

10/524815

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DICTIONARY FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6

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=> file zcaplus

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FILE COVERS 1907 - 14 Oct 2009 VOL 151 ISS 16  
FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

ZCAplus now includes complete International Patent Classification (IPC)  
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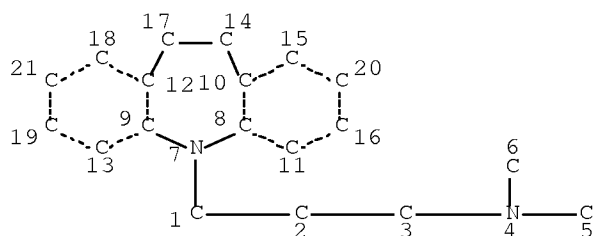
This file contains CAS Registry Numbers for easy and accurate  
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'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L76

L4 STR

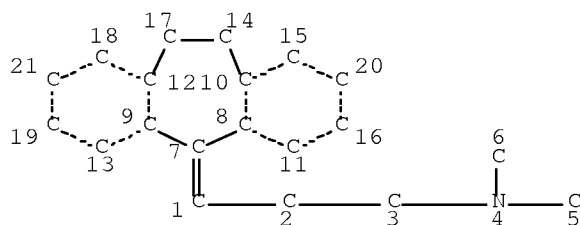
10/524815



NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE  
L5 STR



NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L7 135 SEA FILE=REGISTRY FAM FUL L4  
L9 83 SEA FILE=REGISTRY FAM FUL L5  
L12 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR  
CLOMIPRAMINE OR DOSULEPIN OR DOTHIEPIN OR DOXEPIN OR LOFEPRAMIN  
E OR TRIMIPRAMINE)/CN  
L13 3 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DESIPRAMINE OR  
NORTRIPTYLINE OR PROTRIPTYLINE)/CN  
L14 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR  
DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR  
METAPRAMINE)/CN  
L15 4 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR  
NOXIPTYLINE OR PROPIZEPINE OR QUINUPRAMINE)/CN  
L16 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMINEPTINE OR  
OPIPRAMOL OR TIANEPTINE OR CIANOPRAMINE OR CYANODOTHIEPIN OR  
FLUOTRACEN)/CN  
L17 25 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (L12 OR L13 OR L14

10/524815

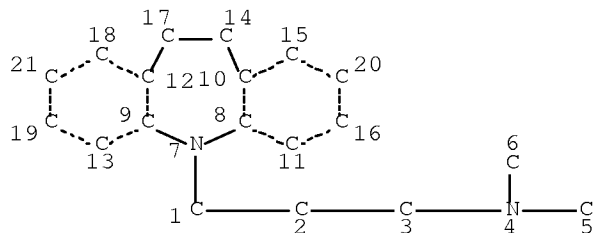
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OR L15 OR L16)
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MAPROTILINE OR MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR
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L75      227 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  GULBINS E?/AU,AUTH
L76      6 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L75 AND (L7 OR L9 OR
L17 OR L19)
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=> d stat que L77

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L25      609 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROCYSTIC?/BI OR
FIBRO CYSTIC?/BI
L26      155 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  MUCOVISCIDOSIS/BI
L27      5892 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  CFTR/BI
L28      15430 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROSIS/BI (L)
CYSTIC/BI
L29      16341 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR
L27 OR L28)
L75      227 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  GULBINS E?/AU,AUTH
L77      18 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L75 AND L29
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=> d stat que L84

L4 STR



NODE ATTRIBUTES:

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DEFAULT ECLEVEL IS LIMITED

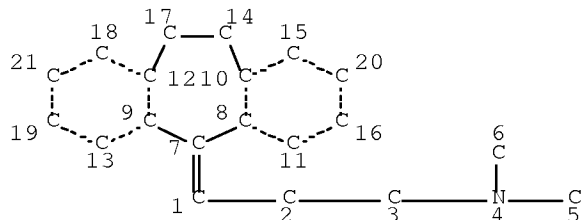
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RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L5 STR



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NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L7 135 SEA FILE=REGISTRY FAM FUL L4  
L9 83 SEA FILE=REGISTRY FAM FUL L5  
L12 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR  
CLOMIPRAMINE OR DOSULEPIN OR DOTHIEPIN OR DOXEPIN OR LOFEPRAMIN  
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L14 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR  
DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR  
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L15 4 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR  
NOXIPTILINE OR PROPIZEPINE OR QUINUPRAMINE)/CN  
L16 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMINEPTINE OR  
OPIPRAMOL OR TIANEPTINE OR CIANOPRAMINE OR CYANODTHIEPIN OR  
FLUOTRACEN)/CN  
L17 25 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (L12 OR L13 OR L14  
OR L15 OR L16)  
L19 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMOXAPINE OR  
MAPROTILINE OR MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR  
OXAPROTILINE)/CN  
L23 36339 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON ANTIDEPRESSANT?/BI OR  
ANTI DEPRESSANT?/BI  
L24 15309 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON ?CYSTIC FIBROS?/BI  
L25 609 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROCYSTIC?/BI OR  
FIBRO CYSTIC?/BI  
L26 155 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON MUCOVISCIDOSIS/BI  
L27 5892 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON CFTR/BI  
L28 15430 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROSIS/BI (L)  
CYSTIC/BI  
L29 16341 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON (L24 OR L25 OR L26 OR  
L27 OR L28)  
L32 9 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON L23 AND (TRICYCLIC?/BI  
OR TETRACYCLIC?/BI) AND L29  
L34 31 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON L17 OR L19  
L36 11 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON L34 AND L29  
L37 12 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON (L7 OR L9) AND L29  
L75 227 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON GULBINS E?/AU,AUTH  
L84 2 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON L75 AND (L32 OR L36  
OR L37)

=> s L76 or L77 or L84

L87 22 L76 OR L77 OR L84

=> file medline embase biosis

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FILE 'EMBASE' ENTERED AT 11:24:54 ON 14 OCT 2009

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FILE 'BIOSIS' ENTERED AT 11:24:54 ON 14 OCT 2009

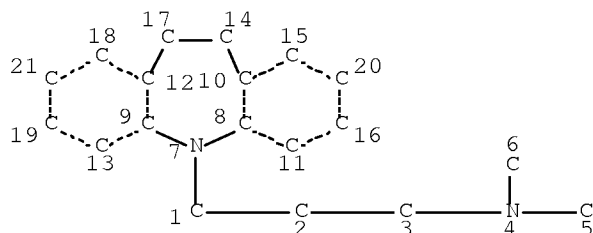


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=> d stat que L78

L4 STR



NODE ATTRIBUTES:

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DEFAULT ECLEVEL IS LIMITED

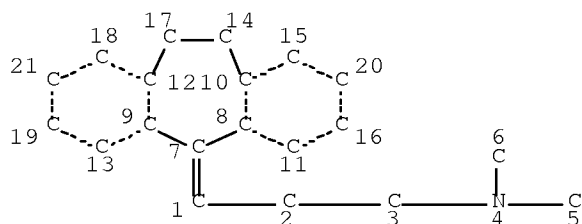
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RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L5 STR



NODE ATTRIBUTES:

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L9 83 SEA FILE=REGISTRY FAM FUL L5

L12 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR CLOMIPRAMINE OR DOSULEPIN OR DOTHIEPIN OR DOXEPIN OR LOFEPRAMINE OR TRIMIPRAMINE)/CN

L13 3 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DESIPRAMINE OR NORTRIPTYLINE OR PROTRIPTYLINE)/CN

L14 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR METAPRAMINE)/CN

L15 4 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR NOXIPTILINE OR PROPIZEPINE OR QUINUPRAMINE)/CN

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L16          6 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (AMINEPTINE OR
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L19          6 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (AMOXAPINE OR
              MAPROTILINE OR MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR
              OXAPROTILINE)/CN
L34          31 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L17 OR L19
L45          218 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L7 OR L9
L46          SEL  PLU=ON  L45 1- CHEM :      409 TERMS
L47          78135 SEA L46
L52          SEL  PLU=ON  L34 1- CHEM :      233 TERMS
L53          91067 SEA L52
L75          227 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  GULBINS E?/AU,AUTH
L78          24 SEA L75 AND (L47 OR L53)

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=> d stat que L79

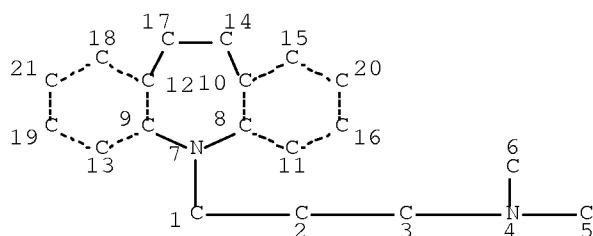
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L25          609 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROCYSTIC?/BI OR
              FIBRO CYSTIC?/BI
L26          155 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  MUCOVISCIDOSIS/BI
L27          5892 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  CFTR/BI
L28          15430 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROSIS/BI (L)
              CYSTIC/BI
L29          16341 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR
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L75          227 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  GULBINS E?/AU,AUTH
L79          48 SEA L75 AND L29

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=> d stat que L82

L4 STR

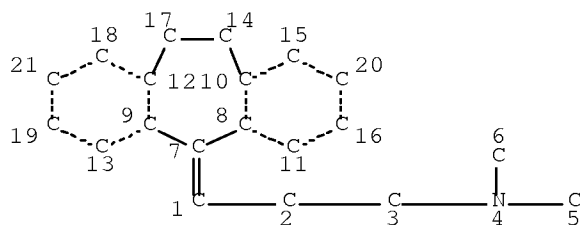


NODE ATTRIBUTES:  
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 DEFAULT ECLEVEL IS LIMITED

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 NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE  
 L5 STR

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NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L7 135 SEA FILE=REGISTRY FAM FUL L4  
 L9 83 SEA FILE=REGISTRY FAM FUL L5  
 L12 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR CLOMIPRAMINE OR DOSULEPIN OR DOTHIEPIN OR DOXEPIN OR LOFEPRAMINE OR TRIMIPRAMINE)/CN  
 L13 3 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DESIPRAMINE OR NORTRIPTYLINE OR PROTRIPTYLINE)/CN  
 L14 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR METAPRAMINE)/CN  
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 L16 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMINEPTINE OR OPIPRAMOL OR TIANEPTINE OR CIANOPRAMINE OR CYANODOTHIEPIN OR FLUOTRACEN)/CN  
 L17 25 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR L16)  
 L19 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMOXAPINE OR MAPROTILINE OR MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR OXAPROTILINE)/CN  
 L24 15309 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON ?CYSTIC FIBROS?/BI  
 L25 609 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROCYSTIC?/BI OR FIBRO CYSTIC?/BI  
 L26 155 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON MUCOVISCIDOSIS/BI  
 L27 5892 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON CFTR/BI  
 L28 15430 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROSIS/BI (L) CYSTIC/BI  
 L29 16341 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28)  
 L34 31 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON L17 OR L19  
 L45 218 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON L7 OR L9  
 L46 SEL PLU=ON L45 1- CHEM : 409 TERMS  
 L47 78135 SEA L46  
 L48 96337 SEA L29  
 L49 39 SEA L47 AND L48  
 L52 SEL PLU=ON L34 1- CHEM : 233 TERMS  
 L53 91067 SEA L52  
 L54 25 SEA L53 AND L29

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L56 24 SEA (TRICYCLIC OR TETRACYCLIC)/BI AND L29  
L57 75 SEA L49 OR L54 OR L56  
L75 227 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON GULBINS E?/AU,AUTH  
L82 8 SEA L57 AND L75

=> s L78 or L79 or L82  
L88 64 L78 OR L79 OR L82

=> dup rem L87 L88  
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FILE 'BIOSIS' ENTERED AT 11:25:25 ON 14 OCT 2009  
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PROCESSING COMPLETED FOR L87  
PROCESSING COMPLETED FOR L88  
L89 37 DUP REM L87 L88 (49 DUPLICATES REMOVED)  
ANSWERS '1-22' FROM FILE ZCAPLUS  
ANSWERS '23-29' FROM FILE MEDLINE  
ANSWERS '30-32' FROM FILE EMBASE  
ANSWERS '33-37' FROM FILE BIOSIS

=> d ibib abs hitind hitstr L89 1-22; d iall L89 23-37

L89 ANSWER 1 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 1  
ACCESSION NUMBER: 2009:173669 ZCAPLUS Full-text  
DOCUMENT NUMBER: 150:188953  
TITLE: Cystic fibrosis and innate immunity: how chloride  
channel mutations provoke lung disease  
AUTHOR(S): Doering, Gerd; Gulbins, Erich  
CORPORATE SOURCE: Institute of Medical Microbiology and Hygiene,  
Tuebingen, 72074, Germany  
SOURCE: Cellular Microbiology (2009), 11(2), 208-216  
CODEN: CEMIF5; ISSN: 1462-5814  
PUBLISHER: Wiley-Blackwell  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review. Innate immunity is essential for prevention of infection in  
vertebrates and plants and dysfunction of single components of innate immunity  
may provoke severe disease. Here we describe how mutations in the cystic  
fibrosis transmembrane conductance regulator gene dysregulate a variety of  
components of the innate immune system in individuals suffering from the  
hereditary disease cystic fibrosis. In the airways of these individuals,  
functions of the mucociliary clearance system, cationic antimicrobial  
(poly)peptides and neutrophils and macrophages are impaired and inflammatory  
signal transduction pathways exaggerated. Consequently, chronic airway  
colonization with opportunistic bacterial pathogens develops and leads to  
life-threatening lung disease.  
CC 15-0 (Immunochemistry)  
Section cross-reference(s): 14  
ST review cystic fibrosis innate immunity chloride channel mutation  
IT CFTR (cystic fibrosis transmembrane

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conductance regulator)

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(chloride channel mutations provoke lung disease)

IT Cystic fibrosis  
(cystic fibrosis and innate immunity)

IT Immunity  
(innate; cystic fibrosis and innate immunity)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 2 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2009:829732 ZCAPLUS Full-text

TITLE: Therapeutic Efficacy and Safety of Amitriptyline in  
Patients with Cystic Fibrosis

AUTHOR(S): Riethmueller, Joachim; Anthonysamy, Janina; Serra,  
Emilio; Schwab, Matthias; Doering, Gerd; Gulbins,  
Erich

CORPORATE SOURCE: Department of Paediatrics, University Hospital  
Tuebingen, Tuebingen, D-72076, Germany

SOURCE: Cellular Physiology and Biochemistry (2009), 24(1-2),  
65-72

CODEN: CEPBEW; ISSN: 1015-8987

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Amitriptyline, a blocker of acid sphingomyelinase and acid ceramidase,  
significantly reduces Pseudomonas aeruginosa lung infection in cystic fibrosis  
(CF) mice with concurrent increase of survival. Our aim was to establish  
whether amitriptyline is safe and effective in the treatment of CF patients.  
In a randomised, double-blinded, placebo-controlled, cross-over pilot study, 4  
adult CF patients received 37.5 mg of amitriptyline or placebo twice daily for  
14 days. Subsequently in a phase II study 19 adult CF patients were randomly  
allocated to three treatment groups receiving amitriptyline once daily for 28  
days at doses of 25 mg (n=7), 50 mg (n=8), or 75 mg (n=8) or placebo (n=13).  
The primary outcome was the difference of forced expiratory volume in 1 s  
(FEV1) at day 14 between amitriptyline and placebo. Primary endpoint measures  
improved significantly in three of four patients in the pilot study after  
amitriptyline treatment vs placebo (relative FEV1: 14.7±5%; p = 0.006) and in  
the 25 mg treatment group of the phase II study (relative FEV1: 4.0±7%; p =  
0.048). Amitriptyline was well tolerated in both studies and 96% of the  
patients completed the studies. Amitriptyline as a novel therapeutic option  
in patients with CF is safe and seems to be efficacious.

CC 1 (Pharmacology)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 3 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2008:1343334 ZCAPLUS Full-text

DOCUMENT NUMBER: 150:18250

TITLE: Ceramide in bacterial infections and cystic fibrosis

AUTHOR(S): Grassme, Heike; Becker, Katrin Anne; Zhang, Yang;  
Gulbins, Erich

CORPORATE SOURCE: Department of Molecular Biology, University of  
Duisburg-Essen, Essen, D-45122, Germany

SOURCE: Biological Chemistry (2008), 389(11), 1371-1379

CODEN: BICHF3; ISSN: 1431-6730

PUBLISHER: Walter de Gruyter GmbH & Co. KG

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Ceramide is formed by the activity of sphingomyelinases, by degradation of complex sphingolipids, reverse ceramidase activity or de novo synthesized. The formation of ceramide within biol. membranes results in the formation of large ceramide-enriched membrane domains. These domains serve the spatial and temporal organization of receptors and signaling mols. The acid sphingomyelinase-ceramide system plays an important role in the infection of mammalian host cells with bacterial pathogens such as Neisseria gonorrhoeae, Escherichia coli, Staphylococcus aureus, Listeria monocytogenes, Salmonella typhimurium and Pseudomonas aeruginosa. Ceramide and ceramide-enriched membrane platforms are also involved in the induction of apoptosis in infected cells, such as in epithelial and endothelial cells after infection with Pseudomonas aeruginosa and Staphylococcus aureus, resp. Finally, ceramide-enriched membrane platforms are critical regulators of the release of pro-inflammatory cytokines upon infection. The diverse functions of ceramide in bacterial infections suggest that ceramide and ceramide-enriched membrane domains are key players in host responses to many pathogens and thus are potential novel targets to treat infections.

CC 14-0 (Mammalian Pathological Biochemistry)

ST review ceramide infection bacteria **cystic fibrosis**

IT Bacterial infection  
Cell membrane  
Cystic fibrosis  
Escherichia coli  
Human  
Listeria monocytogenes  
Mycobacterium  
Neisseria gonorrhoeae  
Pseudomonas aeruginosa  
Salmonella typhimurium  
Staphylococcus aureus  
(ceramide in bacterial infections and **cystic fibrosis**)

IT Ceramides  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ceramide in bacterial infections and **cystic fibrosis**)

IT 9031-54-3, Sphingomyelinase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ceramide in bacterial infections and **cystic fibrosis**)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 4 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2009:58346 ZCAPLUS Full-text

DOCUMENT NUMBER: 150:559646

TITLE: Sphingolipids in the lungs

AUTHOR(S): Uhlig, Stefan; Gulbins, Erich

CORPORATE SOURCE: Institute of Pharmacology and Toxicology, University  
Hospital Aachen, RWTH Aachen, Aachen, Germany

SOURCE: American Journal of Respiratory and Critical Care  
Medicine (2008), 178(11), 1100-1114  
CODEN: AJCMED; ISSN: 1073-449X

PUBLISHER: American Thoracic Society

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Sphingolipids such as sphingosine-1-phosphate (S1P), ceramide, or sphingomyelin are essential constituents of plasma membranes and regulate many

(patho)physiol. cellular responses inducing apoptosis and cell survival, vascular permeability, mast cell activation, and airway smooth muscle functions. The complexity of sphingolipid biol. is generated by a great variety of compds., diverse receptors, and often antagonistic functions of different sphingolipids. For instance, apoptosis is promoted by ceramide and prevented by S1P, and pulmonary vascular permeability is increased by S1P2/3 receptors and by ceramide, whereas S1P1 receptors stabilize barrier integrity. Several enzymes of the sphingolipid metabolism respond to external stimuli such as sphingomyelinase isoenzymes that are activated by many stress stimuli and the sphingosine kinase isoenzymes that are activated by allergens. The past years have provided increasing evidence that these processes contribute to pulmonary disorders including asthma, chronic obstructive pulmonary disease, acute lung injury, and cystic fibrosis. Sphingolipid metabolism offers several novel therapeutic targets for the treatment of lung diseases such as emphysema, asthma, cystic fibrosis, respiratory tract infection, sepsis, and acute lung injury.

CC 14-0 (Mammalian Pathological Biochemistry)

IT Respiratory system disease

(infection; sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Infection

(respiratory tract; sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Stress, biological

(sphingolipid metabolic sphingomyelinase isoenzyme activated by stress stimulus contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)

IT Allergens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(sphingolipid metabolic sphingosine kinase isoenzyme activated by allergen contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)

IT Asthma

Cystic fibrosis

Emphysema

Human

Smooth muscle

(sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Sphingolipids

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Ceramides

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(sphingolipid such as ceramide contributes for lung disorders like emphysema, cystic fibrosis, cystic

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- fibrosis and respiratory tract infection in human)
- IT Sphingomyelins  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(sphingolipid such as sphingomyelin contributes for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)
- IT Apoptosis  
(sphingolipid such as sphingomyelin, spingosine-1-phosphate and ceramide regulates cellular responses inducing apoptosis and contributes for emphysema, cystic fibrosis and respiratory tract infection in human)
- IT Mast cell  
(sphingolipid such as sphingomyelin, spingosine-1-phosphate and ceramide regulates cellular responses inducing mast cell activation and contributes for emphysema, cystic fibrosis and respiratory tract infection in human)
- IT Vascular permeability  
(sphingolipid such as sphingomyelin, spingosine-1-phosphate and ceramide regulates cellular responses inducing vascular permeability and contributes for emphysema, cystic fibrosis and respiratory tract infection in human)
- IT 9031-54-3, Sphingomyelinase  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(sphingolipid metabolic sphingomyelinase isoenzyme activated by stress stimulus contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)
- IT 50864-48-7, Sphingosine kinase  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(sphingolipid metabolic sphingosine kinase isoenzyme activated by allergen contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)

REFERENCE COUNT: 189 THERE ARE 189 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L89 ANSWER 5 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2008:1496580 ZCAPLUS Full-text

DOCUMENT NUMBER: 150:205817

TITLE: Influence of amitriptyline on eryptosis, parasitemia and survival of Plasmodium berghei-infected mice

AUTHOR(S): Brand, Verena; Koka, Saisudha; Lang, Camelia; Jendrossek, Verena; Huber, Stephan M.; Gulbins, Erich; Lang, Florian

CORPORATE SOURCE: Department of Physiology, University of Tuebingen, Germany

SOURCE: Cellular Physiology and Biochemistry (2008), 22(5-6), 405-412

CODEN: CEPBEW; ISSN: 1015-8987

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Plasmodia express a sphingomyelinase, which is apparently required for their development. On the other hand, the sphingomyelinase product ceramide has previously been shown to delay parasite development. Moreover, ceramide triggers suicidal erythrocyte death or eryptosis, characterized by exposure of



phosphatidylserine at the erythrocyte surface and cell shrinkage. Accelerated eryptosis of infected erythrocytes is considered to clear infected erythrocytes from circulating blood and, thus, to favorably influence the clin. course of malaria. The present expts. explored whether the sphingomyelinase inhibitor amitriptyline or genetic knockout of host acid sphingomyelinase influence in vitro parasite growth, eryptosis of *Plasmodium falciparum*-infected human erythrocytes, in vivo parasitemia and survival of *P. berghei*-infected mice. Phosphatidylserine exposure was determined by annexin V-binding and cell volume by forward scatter in FACS anal. In vitro infection of human erythrocytes increased annexin-binding, an effect blunted in the presence of amitriptyline ( $\geq 50 \mu\text{M}$ ). Amitriptyline did not significantly alter intraerythrocytic parasite development but significantly ( $\geq 1 \mu\text{M}$ ) delayed the increase in parasitemia in vitro. Most importantly, amitriptyline treatment (1 mM in drinking water) resulted in a significant delay of parasitemia and death of infected mice. However, upon infection, ceramide formation was stimulated in both, acid sphingomyelinase knockout mice (*Smpdl*<sup>-/-</sup>) and their wild type littermates (*Smpdl*<sup>+/+</sup>). Parasitemia following *P. berghei* infection was significantly lower in *Smpdl*<sup>-/-</sup> than in *Smpdl*<sup>+/+</sup> mice but did not significantly extend the life span of infected animals. In conclusion, mammalian and parasite sphingomyelinase contribute to ceramide formation during malaria, whereby the parasite sphingomyelinase ultimately det. the course of the infection. Amitriptyline presumably blocks both sphingomyelinases and, thus, its use might be a novel strategy to treat malaria.

CC 1-5 (Pharmacology)

IT 50-48-6, Amitriptyline

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amitriptyline inhibits host and parasite sphingomyelinase in *Plasmodium berghei*-infected mice)

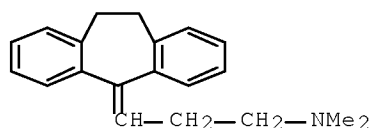
IT 50-48-6, Amitriptyline

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amitriptyline inhibits host and parasite sphingomyelinase in *Plasmodium berghei*-infected mice)

RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 6 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2008:439128 ZCAPLUS Full-text

DOCUMENT NUMBER: 149:6518

TITLE: Ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis

10/524815

AUTHOR(S): Teichgraeber, Volker; Ulrich, Martina; Endlich, Nicole; Riethmueller, Joachim; Wilker, Barbara; De Oliveira-Munding, Cheyla Conceicao; van Heeckeren, Anna M.; Barr, Mark L.; von Kuerthy, Gabriele; Schmid, Kurt W.; Weller, Michael; Tuemmler, Burkhard; Lang, Florian; Grassme, Heike; Doering, Gerd; Gulbins, Erich

CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Essen, 45122, Germany

SOURCE: Nature Medicine (New York, NY, United States) (2008), 14(4), 382-391  
CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Microbial lung infections are the major cause of morbidity and mortality in the hereditary metabolic disorder *cystic fibrosis*, yet the mol. mechanisms leading from the mutation of *cystic fibrosis* transmembrane conductance regulator (CFTR) to lung infection are still unclear. Here, we show that ceramide age-dependently accumulates in the respiratory tract of uninfected Cftr-deficient mice owing to an alkalization of intracellular vesicles in Cftr-deficient cells. This change in pH results in an imbalance between acid sphingomyelinase (Asm) cleavage of sphingomyelin to ceramide and acid ceramidase consumption of ceramide, resulting in the higher levels of ceramide. The accumulation of ceramide causes Cftr-deficient mice to suffer from constitutive age-dependent pulmonary inflammation, death of respiratory epithelial cells, deposits of DNA in bronchi and high susceptibility to severe *Pseudomonas aeruginosa* infections. Partial genetic deficiency of Asm in Cftr-/-Smpdl+/- mice or pharmacol. treatment of Cftr-deficient mice with the Asm blocker amitriptyline normalizes pulmonary ceramide and prevents all pathol. findings, including susceptibility to infection. These data suggest inhibition of Asm as a new treatment strategy for *cystic fibrosis*.

CC 14-4 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 1

ST ceramide inflammation infection susceptibility *cystic fibrosis*

IT *Cystic fibrosis*  
Human  
Pneumonitis  
*Pseudomonas aeruginosa*  
Respiratory system  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in *cystic fibrosis*)

IT CFTR (*cystic fibrosis* transmembrane conductance regulator)  
Ceramides  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in *cystic fibrosis*)

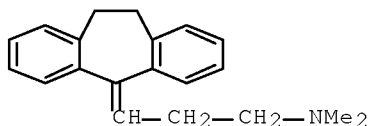
IT Sphingomyelins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in *cystic fibrosis*)

IT DNA  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(deposits in respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in *cystic fibrosis*)

IT Respiratory system  
(epithelium, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in *cystic*

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- fibrosis)
- IT Apoptosis  
(of respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Epithelium  
(respiratory tract, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Organelle  
(vesicle, alkalinization of; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 57-88-5, Cholesterol, biological studies 123-78-4, Sphingosine 9031-54-3, Acid sphingomyelinase 26993-30-6, Sphingosine 1-phosphate 37289-06-8, Acid ceramidase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 212059-03-5, Peptamen  
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 50-48-6, Amitriptyline  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 50-48-6, Amitriptyline  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 7 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 8  
ACCESSION NUMBER: 2008:1066216 ZCAPLUS Full-text  
DOCUMENT NUMBER: 149:439268  
TITLE: DNA Quantification and Fragmentation in Sputum after Inhalation of Recombinant Human Deoxyribonuclease  
AUTHOR(S): Riethmueller, Joachim; Vonthein, Reinhard; Borth-Bruhns, Thomas; Grassme, Heike; Eyrich, Matthias; Schilbach, Karin; Stern, Martin; Gulbins, Erich

10/524815

CORPORATE SOURCE: Department of Pediatrics, Tuebingen University  
Hospital, Tuebingen, D-72076, Germany  
SOURCE: Cellular Physiology and Biochemistry (2008), 22(1-4),  
347-352  
CODEN: CEPBEW; ISSN: 1015-8987  
PUBLISHER: S. Karger AG  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Inhaled rhDNase may improve sputum viscosity and mucociliary clearance by cleavage of extracellular DNA derived for instance from dead leukocytes in purulent, highly viscous patient sputum. Here we established a method to quantify rhDNase-mediated DNA fragmentation in sputum using gel electrophoresis. Sputum of *Pseudomonas aeruginosa* colonized cystic fibrosis (CF) patients with (CF+) or without (CF-) rhDNase treatment or mech. ventilated non-CF patients receiving rhDNase (non-CF+) or not (non-CF-) was analyzed. DNA measurements from T-lymphocytes served as controls. Absolute DNA content and the relative quantity within eight mol. mass ranges (12000 to 200 bp) was determined by gel electrophoresis and densitometric anal. Geometric mean sputum DNA concns. were 0.41 mg/dL for CF- (n=54), 0.78 mg/dL for CF+ (n=60), 0.053 mg/dL for non-CF- (n=41) and 0.049 mg/dL for non-CF+ (n=28). Treatment with rhDNase resulted in fragmentation of DNA that was quantified by separation and densitometric anal. of the DNA on agarose gels. The new anal. method permits anal. of DNA cleavage with high accuracy. This new monitoring method facilitates DNA quantification and in vitro monitoring of rhDNase in sputum.

CC 1-1 (Pharmacology)

IT Cystic fibrosis

DNA fragmentation

Expectorants

Gel electrophoresis

Human

Sputum

Therapeutic drug monitoring

(DNA quantification and fragmentation in sputum after inhalation of recombinant human DNase)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 8 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2007:1330373 ZCAPLUS Full-text

DOCUMENT NUMBER: 148:112291

TITLE: Identification of New Functional Inhibitors of Acid  
Sphingomyelinase Using a Structure-Property-Activity  
Relation Model

AUTHOR(S): Kornhuber, Johannes; Tripal, Philipp; Reichel, Martin;  
Terfloth, Lothar; Bleich, Stefan; Wiltfang, Jens;  
Gulbins, Erich

CORPORATE SOURCE: Department of Psychiatry and Psychotherapy, University  
of Erlangen, Erlangen, D-91054, Germany

SOURCE: Journal of Medicinal Chemistry (2008), 51(2), 219-237  
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

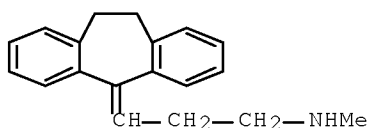
DOCUMENT TYPE: Journal

LANGUAGE: English

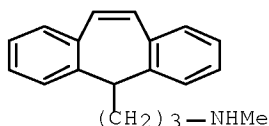
AB Some organic weak bases induce a detachment from inner lysosomal membranes and subsequent inactivation of acid sphingomyelinase (ASM) and thus work as functional ASM inhibitors. The aim of the present investigation was to develop a structure-property-activity relation (SPAR) model in order to

specify the structural and physicochem. characteristics of probes capable of functionally inhibiting ASM. High pKa and high log P values are necessary but not sufficient preconditions for functional inhibition of ASM. The exptl. data supported the requirement of an addnl. factor, which is necessary for functional inhibition of ASM. This factor k is related to the steric hindrance of the most basic nitrogen atom and presumably modulates the free presentation of a protonated nitrogen atom at the inner lysosomal surface. During the course of the study, the authors characterized 26 new functional ASM inhibitors, including doxepine 63, fluoxetine 104, maprotiline 109, nortriptyline 114, paroxetine 118, sertraline 124, suloctidil 125, and terfenadine 127.

CC 1-3 (Pharmacology)  
 IT 54-30-8, Camylofin 58-40-2, Promazine 60-87-7, Promethazine 72-69-5, Nortriptyline 86-13-5, Benztropine 113-59-7, Chlorprothixene 129-03-3, Cyproheptadine 146-54-3, Triflupromazine 303-53-7, Cyclobenzaprine 314-03-4, Pimethixene 438-60-8, Protriptyline 911-45-5, Clomiphene 1668-19-5, Doxepine 1679-76-1, Drofenine 3703-76-2, Cloperastine 10262-69-8, Maprotiline 13042-18-7, Fendiline 50679-08-8, Terfenadine 54767-75-8, Suloctidil 54910-89-3, Fluoxetine 61869-08-7, Paroxetine 64706-54-3, Bepridil 68844-77-9, Astemizole 79617-96-2, Sertraline 83891-03-6, Norfluoxetine 88150-42-9, Amlodipine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (identification of new functional inhibitors of acid sphingomyelinase using a structure-property-activity relation model)  
 IT 72-69-5, Nortriptyline 438-60-8, Protriptyline 1668-19-5, Doxepine 10262-69-8, Maprotiline  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (identification of new functional inhibitors of acid sphingomyelinase using a structure-property-activity relation model)  
 RN 72-69-5 ZCAPLUS  
 CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



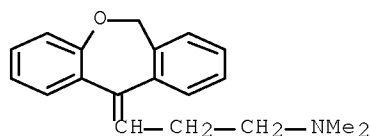
RN 438-60-8 ZCAPLUS  
 CN 5H-Dibenzo[a,d]cycloheptene-5-propanamine, N-methyl- (CA INDEX NAME)



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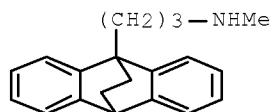
RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



RN 10262-69-8 ZCAPLUS

CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 9 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 2007:1284150 ZCAPLUS Full-text

DOCUMENT NUMBER: 148:50999

TITLE: Ceramide in Pseudomonas aeruginosa infections

AUTHOR(S): Riethmueller, Joachim; Riehle, Andrea; Grassme, Heike; Gulbins, Erich

CORPORATE SOURCE: Children's Hospital, University of Tuebingen, Tuebingen, Germany

SOURCE: European Journal of Lipid Science and Technology (2007), 109(10), 998-1002

CODEN: EJLTFM; ISSN: 1438-7697

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Cystic fibrosis (CF), the most common autosomal recessive disorder, at least in western countries, is caused by mutations of the cystic fibrosis transmembranous conductance regulator (CFTR) mol. and affects approx. 80,000 patients in Europe and the USA. Most, if not all, CF patients develop a chronic pulmonary infection with Pseudomonas aeruginosa. At present it is unknown why CF patients are highly sensitive to P. aeruginosa infections, and most importantly, no curative treatment for CF is available. P. aeruginosa infection results in an activation of the enzyme acid sphingomyelinase which catalyzes the release of ceramide from sphingomyelin in the cell membrane. Ceramide forms large ceramide-enriched membrane domains that are required for internalization of bacteria, induction of cell death in infected cells and a controlled release of cytokines from infected cells. Ceramide-enriched membrane platforms seem to serve the reorganization of receptors and

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intracellular signaling molcs. involved in the infection of mammalian cells with *P. aeruginosa*. The significance of the acid sphingomyelinase and ceramide for the infection of mammalian cells with *P. aeruginosa* was demonstrated on mice genetically deficient for the acid sphingomyelinase. Further studies with *N. gonorrhoeae*, *S. aureus* and rhinoviruses indicate that ceramide-enriched membrane domains are also important for the infection of mammalian cells with other bacterial and viral pathogens, suggesting a general role of these membrane domains in infectious biol.

CC 14-0 (Mammalian Pathological Biochemistry)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 10 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2006:132218 ZCAPLUS Full-text

DOCUMENT NUMBER: 144:290514

TITLE: Phospholipase A2 functions in *Pseudomonas aeruginosa*-induced apoptosis

AUTHOR(S): Kirschnek, Susanne; Gulbins, Erich

CORPORATE SOURCE: Department of Medical Microbiology, Technische Universitat Munich, Munich, 81675, Germany

SOURCE: Infection and Immunity (2006), 74(2), 850-860

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Pseudomonas aeruginosa*, a gram-neg., facultative pathogen, causes severe and often even lethal infections in immunocompromised patients, as well as cystic fibrosis patients. We show here that a variety of *P. aeruginosa* strains activate phospholipase A2 (PLA2), cultured epithelial cells, and fibroblasts, resulting in increased intracellular and extracellular arachidonic acid release. The use of different PLA2 inhibitors revealed that *P. aeruginosa*-induced arachidonic acid release is mediated by activation of cytosolic PLA2 (cPLA2), whereas iPLA2 or sPLA2 do not seem to be involved in the response to *P. aeruginosa*. Likewise, the cPLA2-specific inhibitors MAFP and AACOCF3 prevented apoptosis of cultured epithelial cells upon *P. aeruginosa* infection, whereas inhibitors specific for iPLA2 or sPLA2 were without effect. The physiol. significance of these findings is indicated by an inhibition of apoptosis in tracheal epithelial cells upon in vivo infection with *P. aeruginosa*. The data indicate that arachidonic acid generation by activation of cPLA2 during *P. aeruginosa* infection plays an important role in the induction of host cell death.

CC 14-4 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 10

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 11 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 2005:1138242 ZCAPLUS Full-text

DOCUMENT NUMBER: 144:184461

TITLE: High activity of acid sphingomyelinase in major depression

AUTHOR(S): Kornhuber, J.; Medlin, A.; Bleich, S.; Jendrossek, V.; Henkel, A. W.; Wiltfang, J.; Gulbins, E.

CORPORATE SOURCE: Department of Psychiatry, University of Erlangen, Germany

SOURCE: Journal of Neural Transmission (2005), 112(11), 1583-1590

CODEN: JNTRF3; ISSN: 0300-9564

10/524815

PUBLISHER: Springer Wien  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Acid sphingomyelinase (A-SMase) and its reaction product ceramide may play a role in the pathophysiol. of depressive disorders and in the therapeutic action of antidepressive drugs. In a prospective case-control study, A-SMase activity was measured in peripheral blood mononuclear cells of 17 patients with a major depressive episode who were free of antidepressant drug therapy for at least 10 days and 8 healthy volunteers. In the patient group, A-SMase activity was correlated to the score ( $n = 17$ ,  $r = 0.64$ ,  $P = 0.005$ ). The patient group exhibited higher A-SMase activity compared to healthy volunteers ( $T = 2.09$ ,  $df = 21.33$ ,  $P < 0.05$ ). In addition, we demonstrate that the antidepressants imipramine and amitriptyline induce a long-term reduction of the activity of A-SMase in cultured cells.

CC 1-11 (Pharmacology)

IT 50-48-6, Amitriptyline

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(amitriptyline induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)

IT 50-49-7, Imipramine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(imipramine induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)

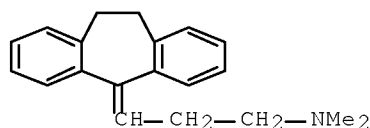
IT 50-48-6, Amitriptyline

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(amitriptyline induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)

RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



IT 50-49-7, Imipramine

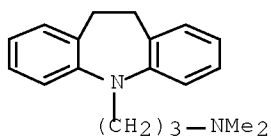
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(imipramine induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)

RN 50-49-7 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)





OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 12 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 13

ACCESSION NUMBER: 2005:45517 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:294587

TITLE: Annexin II is a novel receptor for *Pseudomonas aeruginosa*

AUTHOR(S): Kirschnek, Susanne; Adams, Constantin; Gulbins, Erich

CORPORATE SOURCE: Department of Medical Microbiology, Technical University Munich, Munich, 81675, Germany

SOURCE: Biochemical and Biophysical Research Communications (2005), 327(3), 900-906

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Infections with *P. aeruginosa* are critical in ventilated and poly-traumatized patients. Most important, these bacteria cause frequent and chronic pulmonary infections in patients with cystic fibrosis. Therefore, identification of mol. mechanisms that mediate the infection of mammalian cells with *P. aeruginosa* is urgently required. Here, we aimed to identify novel receptors that are involved in internalization of *P. aeruginosa* into mammalian epithelial cells. Employing SDS-PAGE purification and mass spectrometry we demonstrate that annexin II specifically binds to *P. aeruginosa*. The significance of the interaction of annexin II with *P. aeruginosa* for the infection of mammalian cells is indicated by the finding that neutralization of the ligands on *P. aeruginosa* by incubation of the bacteria with recombinant, soluble annexin II prevents internalization of *P. aeruginosa* into human epithelial cells.

CC 10-6 (Microbial, Algal, and Fungal Biochemistry)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 13 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 14

ACCESSION NUMBER: 2003:155313 ZCAPLUS Full-text

DOCUMENT NUMBER: 138:270184

TITLE: Host defense against *Pseudomonas aeruginosa* requires ceramide-rich membrane rafts

AUTHOR(S): Grassme, H.; Jendrossek, V.; Riehle, A.; von Kuerthy, G.; Berger, J.; Schwarz, H.; Weller, M.; Kolesnick, R.; Gulbins, E.

CORPORATE SOURCE: Department of Molecular Biology, University of Essen, Essen, Germany

SOURCE: Nature Medicine (New York, NY, United States) (2003), 9(3), 322-330

CODEN: NAMEFI; ISSN: 1078-8956

10/524815

PUBLISHER: Nature Publishing Group  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Pseudomonas aeruginosa infection is a serious complication in patients with cystic fibrosis and in immunocompromised individuals. Here the authors show that P. aeruginosa infection triggers activation of the acid sphingomyelinase and the release of ceramide in sphingolipid-rich rafts. Ceramide reorganizes these rafts into larger signaling platforms that are required to internalize P. aeruginosa, induce apoptosis and regulate the cytokine response in infected cells. Failure to generate ceramide-enriched membrane platforms in infected cells results in an unabated inflammatory response, massive release of interleukin (IL)-1 and septic death of mice. These findings show that ceramide-enriched membrane platforms are central to the host defense against this potentially lethal pathogen.

CC 15-8 (Immunochemistry)

Section cross-reference(s): 10

IT CFTR (cystic fibrosis transmembrane conductance regulator)

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(clustering in mouse tracheal epithelium by Pseudomonas aeruginosa infection)

IT Cystic fibrosis

(host defense against Pseudomonas aeruginosa requires ceramide-rich membrane rafts in relation to)

OS.CITING REF COUNT: 147 THERE ARE 147 CAPLUS RECORDS THAT CITE THIS RECORD (147 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 14 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 15

ACCESSION NUMBER: 2001:240652 ZCAPLUS Full-text

DOCUMENT NUMBER: 135:17827

TITLE: Pseudomonas aeruginosa-induced apoptosis involves mitochondria and stress-activated protein kinases

AUTHOR(S): Jendrossek, Verena; Grassme, Heike; Mueller, Ilka; Lang, Florian; Gulbins, Erich

CORPORATE SOURCE: Department of Physiology, University of Tuebingen, Tuebingen, 72076, Germany

SOURCE: Infection and Immunity (2001), 69(4), 2675-2683

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pseudomonas aeruginosa, a gram-neg. facultative pathogen, causes severe infections in immunocompromised and cystic fibrosis patients. However, the mol. details of the interaction between P. aeruginosa and mammalian cells are still largely unknown. Here, infection of human conjunctiva epithelial Chang cells with the well-characterized P. aeruginosa strain PAO-I resulted in rapid induction of apoptosis. Apoptosis was mediated by mitochondrial alterations, in particular mitochondrial depolarization, synthesis of reactive oxygen intermediates, and release of cytochrome c, as well as an activation of Jun N-terminal kinases (JNK). Stimulation of these events was dependent on upregulation of CD95 on infected cells, and a deficiency of CD95 or the CD95 ligand prevented mitochondrial changes, JNK activation, and apoptosis upon infection. Further, efficient apoptosis of Chang epithelial cells required infection with live P. aeruginosa, adhesion but not invasion of the bacteria, and expression of the type III secretion system in PAO-I. The data indicate a type III secretion system-dependent, sequential activation of several signaling pathways by P. aeruginosa PAO-I, resulting in apoptosis of the infected cell.

10/524815

CC 14-3 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 10  
IT Apoptosis  
Cell adhesion  
Cystic fibrosis  
Immunodeficiency  
Mitochondria  
Pseudomonas aeruginosa  
Signal transduction, biological  
(Pseudomonas aeruginosa infection of epithelial cells induces apoptosis  
via P. aeruginosa's type III secretion system which upregulates CD95  
and stimulates JNK and mitochondrial alterations)  
OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS  
RECORD (44 CITINGS)  
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 15 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 16

ACCESSION NUMBER: 2001:20256 ZCAPLUS Full-text  
DOCUMENT NUMBER: 134:205873  
TITLE: Invasion of human epithelial cells by Pseudomonas  
aeruginosa involves Src-like tyrosine kinases p60Src  
and p59Fyn  
AUTHOR(S): Esen, Meral; Grassme, Heike; Riethmuller, Joachim;  
Riehle, Andrea; Fassbender, Klaus; Gulbins, Erich  
CORPORATE SOURCE: Department of Physiology, University of Tuebingen,  
Tuebingen, 72076, Germany  
SOURCE: Infection and Immunity (2001), 69(1), 281-287  
CODEN: INFIBR; ISSN: 0019-9567  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Pseudomonas aeruginosa plays a major role in respiratory tract infections or  
sepsis in patients with cystic fibrosis or upon suppression of the immune  
system. Several P. aeruginosa strains have been shown to be internalized by  
human epithelial cells; however, the mol. mechanisms of the invasion process  
are poorly characterized. Here, the internalization of P. aeruginosa into  
human epithelial cells resulted in and required activation of the Src-like  
tyrosine kinases p59Fyn and p60Src and the consequent tyrosine phosphorylation  
of several eukaryotic proteins. The significance of Src-like tyrosine kinase  
activation is shown by an almost complete blockade of P. aeruginosa  
internalization, but not adhesion, upon inhibition of Src-like tyrosine  
kinases. Likewise, inhibition of P. aeruginosa binding to CFTR, which has  
been shown to block P. aeruginosa internalization, prevents Src and Fyn  
activation, supporting a pivotal role of Src-like tyrosine kinases for  
invasion by P. aeruginosa.

CC 14-3 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 10

IT Cell adhesion  
Cystic fibrosis  
Pseudomonas aeruginosa  
Sepsis  
(invasion of human pulmonary epithelial cells by Pseudomonas aeruginosa  
involves Src-like tyrosine kinases p60Src and p59Fyn)

IT CFTR (cystic fibrosis transmembrane  
conductance regulator)  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)  
(invasion of human pulmonary epithelial cells by Pseudomonas aeruginosa  
involves Src-like tyrosine kinases p60Src and p59Fyn)

10/524815

OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS  
RECORD (32 CITINGS)  
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 16 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 17  
ACCESSION NUMBER: 2000:763385 ZCAPLUS Full-text  
DOCUMENT NUMBER: 133:347707  
TITLE: Physiology of apoptosis  
AUTHOR(S): Gulbins, E.; Jekle, A.; Ferlinz, K.; Grassme, H.;  
Lang, F.  
CORPORATE SOURCE: Department of Physiology, University of Tuebingen,  
Tuebingen, 72076, Germany  
SOURCE: American Journal of Physiology (2000), 279(4, Pt. 2),  
F605-F615  
CODEN: AJPHAP; ISSN: 0002-9513  
PUBLISHER: American Physiological Society  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 113 refs. Ion fluxes and volume changes of the whole cell as well as of organelles belong to the hallmarks of apoptosis; however, the mol. mechanism regulating these changes is only poorly characterized. Several ion channels in the plasma membrane, in particular the N-type K<sup>+</sup> channel, the chloride channel cystic fibrosis conductance regulator, and an outward rectifying chloride channel, as well as the mitochondrial permeability transition pore, have been implicated to be involved in signal transduction cascades regulating apoptosis. Furthermore, Bcl-2-like proteins have been suggested to function, at least in part, as ion channels, because they display some homol. to bacterial pore-forming toxins. In contrast to the demonstration of the involvement of these different ion channels in apoptosis, the mol. consequences regulated by these ion channels, and finally triggering apoptosis, are almost completely unknown.

CC 13-0 (Mammalian Biochemistry)

OS.CITING REF COUNT: 68 THERE ARE 68 CAPLUS RECORDS THAT CITE THIS  
RECORD (68 CITINGS)  
REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L89 ANSWER 17 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 18  
ACCESSION NUMBER: 2001:322701 ZCAPLUS Full-text  
DOCUMENT NUMBER: 135:58810  
TITLE: Tyrosine kinases open lymphocyte chloride channels  
AUTHOR(S): Lepple-Wienhues, Albrecht; Szabo, Ildiko; Wieland,  
Ulrich; Heil, Luzia; Gulbins, Erich; Lang, Florian  
CORPORATE SOURCE: Department of Physiology I, University of Tübingen,  
Tübingen, Germany  
SOURCE: Cellular Physiology and Biochemistry (2000), 10(5-6),  
307-312  
CODEN: CEPBEW; ISSN: 1015-8987  
PUBLISHER: S. Karger AG  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 41 refs. Osmotic swelling of lymphocytes opens outwardly rectifying Cl<sup>-</sup> channels (ORCC) through the src-like kinase p56lck. The central role of this tyrosine protein kinase has been shown by genetic and pharmacol. manipulation of the enzyme. Furthermore, p56lck activates ORCC independently of cell volume increase. ORCC in lymphocytes and epithelial cells from cystic fibrosis (CF) patients are resistant to activation by cAMP. However, osmotic swelling as well as intracellular purified p56lck can

activate ORCC in CF lymphocytes. In non-CF lymphocytes ORCC is opened by either, intracellular cAMP, p56lck or by osmotic swelling. Osmotic activation of ORCC can be blocked by the tyrosine kinase inhibitor lavendustin in both cell types. Regulation of ORCC by p56lck thus represents an alternative pathway of stimulating membrane chloride conductance that is left functional in cystic fibrosis. In addition to osmoregulation these mechanisms could play a major role when cells actively change their volume, i.e. during proliferation and apoptosis. Activation of the tyrosine kinase p56lck is an important regulatory step for opening of chloride channels in lymphocytes.

CC 13-0 (Mammalian Biochemistry)

Section cross-reference(s): 14

ST review lck tyrosine kinase chloride channel osmotic apoptosis lymphocyte;  
cystic fibrosis chloride channel tyrosine kinase review

IT Cystic fibrosis

(tyrosine kinases, cAMP and osmotic swelling in regulation of  
lymphocyte chloride channels in relation to)

OS.CITING REF COUNT: 30 THERE ARE 30 CAPLUS RECORDS THAT CITE THIS  
RECORD (30 CITINGS)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 18 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:827242 ZCAPLUS Full-text

DOCUMENT NUMBER: 151:108500

TITLE: Pharmaceutical composition for prophylaxis and/or  
symptomatic treatment of cystic fibrosis with  
antidepressants

INVENTOR(S): Gulbins, Erich

PATENT ASSIGNEE(S): Cycnad GmbH & Co. KG, Germany

SOURCE: PCT Int. Appl., 54pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009083211	A2	20090709	WO 2008-EP10996	20081222
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
PRIORITY APPLN. INFO.:			DE 2007-102007063535A	20071221

AB The invention relates to a pharmaceutical compound for the prophylaxis and/or symptomatic treatment of cystic fibrosis, particularly for the prophylaxis and/or treatment of infections and/or infection illnesses manifesting with cystic fibrosis, having at least one anti-depressive and preferable at least one dispersion agent and/or at least one pharmaceutically tolerated carrier material. Liquid dispersion media are used to prepare parenteral, especially inhalant delivery systems. Thus Cfr-knockout mice and wild-type mice were

treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration

IC ICM A61K

CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1, 14

ST ~~cystic fibrosis~~ antidepressant inhalant

IT 5-HT reuptake inhibitors  
Antidepressants  
Burkholderia cepacia  
Cystic fibrosis  
Dopamine reuptake inhibitors  
Haemophilus influenzae  
Inhalation drug delivery systems  
Lung  
Noradrenaline reuptake inhibitors  
Parenteral drug delivery systems  
Pharmaceutical solutions  
Prophylaxis  
Pseudomonas aeruginosa  
Staphylococcus aureus  
Therapy  
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of ~~cystic fibrosis~~ with antidepressants)

IT Antibodies and Immunoglobulins  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of ~~cystic fibrosis~~ with antidepressants)

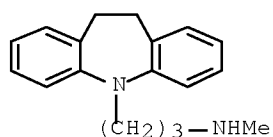
IT 111-57-9, Ceramid 9031-54-3, Sphingomyelinase  
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)  
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of ~~cystic fibrosis~~ with antidepressants)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenalin 51-61-6, Dopamine, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of ~~cystic fibrosis~~ with antidepressants)

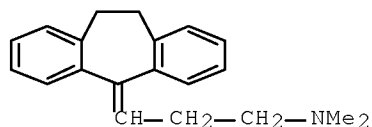
IT 50-47-5, Desipramine 50-48-6, Amitriptyline  
50-49-7, Imipramine 58-40-2, Promazine 72-69-5,  
Nortriptyline 86-13-5, Benztropine 113-45-1, Methylphenidate  
129-03-3, Cyproheptadine 155-09-9, Tranylcypromine 256-96-2D,  
5H-Dibenz[b,f]azepine, derivative 303-49-1 303-53-7,  
Cyclobenzaprine 315-72-0 494-19-9,  
10,11-Dihydro-5H-dibenzo[b,f]azepine 739-71-9, Trimipramine  
911-45-5, Clomiphen 1668-19-5, Doxepine 4317-14-0,  
Amitriptyline oxide 4498-32-2, Dibenzepine 6621-47-2,  
Perhexiline 10262-69-8, Maprotiline 19794-93-5, Trazodon  
23047-25-8, Lofepramine 24219-97-4, Mianserin  
24526-64-5, Nomifensin 32359-34-5, Medifoxamine 34911-55-2, Bupropion  
46817-91-8, Viloxazine 54739-18-3, Fluvoxamine 57574-09-1,  
Amineptine 59729-33-8, Citalopram 61869-08-7, Paroxetine 71320-77-9,  
Moclobemide 71620-89-8, Reboxetine 72797-41-2, Tianeptine  
83366-66-9, Nefazodone 85650-52-8, Mirtazapine 92623-85-3,  
Milnacipran 93413-69-5, Venlafaxin 116539-59-4, Duloxetine  
128196-01-0, Escitalopram  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of ~~cystic fibrosis~~ with antidepressants)

10/524815

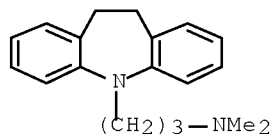
IT 50-47-5, Desipramine 50-48-6, Amitriptyline  
50-49-7, Imipramine 72-69-5, Nortriptyline  
303-49-1 315-72-0 739-71-9, Trimipramine  
1668-19-5, Doxepine 4498-32-2, Dibenzepine  
10262-69-8, Maprotiline 23047-25-8, Lofepramine  
24219-97-4, Mianserin 57574-09-1, Amineptine  
72797-41-2, Tianeptine 85650-52-8, Mirtazapine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of  
cystic fibrosis with antidepressants)  
RN 50-47-5 ZCAPLUS  
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (CA INDEX  
NAME)



RN 50-48-6 ZCAPLUS  
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-  
dimethyl- (CA INDEX NAME)

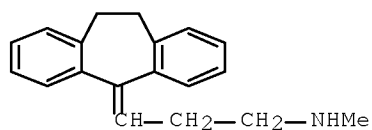


RN 50-49-7 ZCAPLUS  
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA  
INDEX NAME)



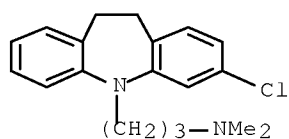
RN 72-69-5 ZCAPLUS  
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-  
methyl- (CA INDEX NAME)

10/524815



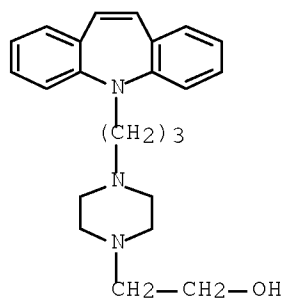
RN 303-49-1 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl-  
(CA INDEX NAME)



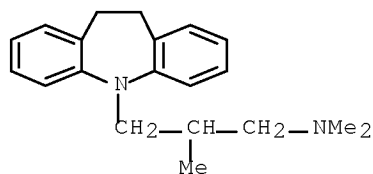
RN 315-72-0 ZCAPLUS

CN 1-Piperazineethanol, 4-[3-(5H-dibenz[b,f]azepin-5-yl)propyl]- (CA INDEX  
NAME)



RN 739-71-9 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N,β-trimethyl-  
(CA INDEX NAME)

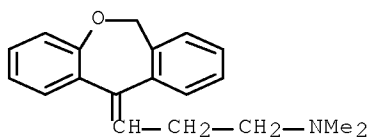


RN 1668-19-5 ZCAPLUS



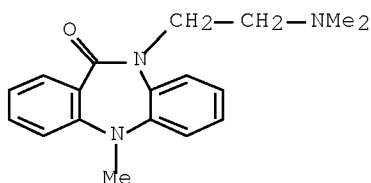
10/524815

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



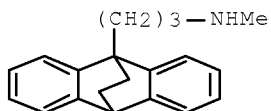
RN 4498-32-2 ZCAPLUS

CN 11H-Dibenzo[b,e][1,4]diazepin-11-one, 10-[2-(dimethylamino)ethyl]-5,10-dihydro-5-methyl- (CA INDEX NAME)



RN 10262-69-8 ZCAPLUS

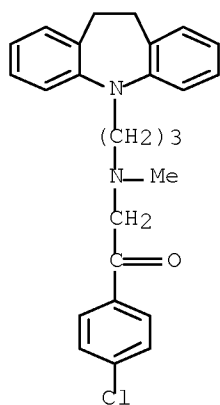
CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



RN 23047-25-8 ZCAPLUS

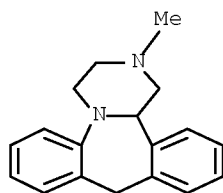
CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]methylamino]- (CA INDEX NAME)

10/524815



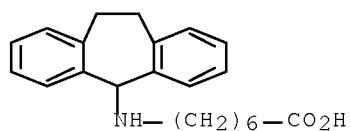
RN 24219-97-4 ZCAPLUS

CN Dibenzo[c,f]pyrazino[1,2-a]azepine, 1,2,3,4,10,14b-hexahydro-2-methyl-  
(CA INDEX NAME)



RN 57574-09-1 ZCAPLUS

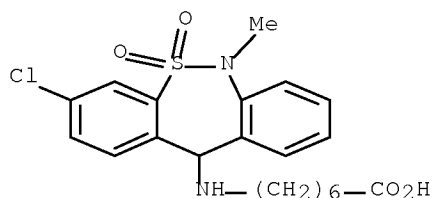
CN Heptanoic acid, 7-[(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)amino]-  
(CA INDEX NAME)



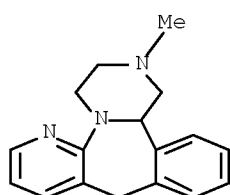
RN 72797-41-2 ZCAPLUS

CN Heptanoic acid, 7-[(3-chloro-6,11-dihydro-6-methyl-5,5-dioxidodibenzo[c,f][1,2]thiazepin-11-yl)amino]- (CA INDEX NAME)

10/524815



RN 85650-52-8 ZCAPLUS  
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine,  
1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



L89 ANSWER 19 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2009:891218 ZCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 151:120391  
TITLE: Cystic fibrosis - pathophysiological concepts  
AUTHOR(S): Becker, Katrin Anne; Riethmueller, Joachim; Doering, Gerd; Gulbins, Erich  
CORPORATE SOURCE: Institut fuer Molekularbiologie, Universitaetsklinikum  
Essen, Universitaet Duisburg-Essen, Essen, Germany  
SOURCE: BIOSpektrum (2009), 15(4), 383-385  
CODEN: BOSPFD; ISSN: 0947-0867  
PUBLISHER: Spektrum Akademischer Verlag GmbH  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: German  
AB A review. Cystic fibrosis patients very often suffer from chronic pulmonary infections, in particular with Pseudomonas aeruginosa. The mol. mechanisms of the very high infection susceptibility of these patients are presently unknown.  
CC 14-0 (Mammalian Pathological Biochemistry)  
ST review cystic fibrosis ceramide pathophysiol chronic infection  
IT Lung disease  
(chronic, infection; cystic fibrosis, ceramides in pathophysiol., and chronic infections)  
IT Cystic fibrosis  
Human  
(cystic fibrosis, ceramides in pathophysiol., and chronic infections)  
IT Ceramides  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cystic fibrosis, ceramides in pathophysiol., and chronic infections)  
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

L89 ANSWER 20 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:177956 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:193037

TITLE: Use of inhibitors of acid sphingomyelinase and of acid sphingomyelinase reaction products for the prophylaxis and treatment of infectious diseases

INVENTOR(S): Gulbins, Erich

PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 10 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10239531	A1	20040304	DE 2002-10239531	20020823
CA 2497582	A1	20040304	CA 2003-2497582	20030821
WO 2004017949	A2	20040304	WO 2003-EP9254	20030821
WO 2004017949	A3	20040429		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003255468	A1	20040311	AU 2003-255468	20030821
EP 1531826	A2	20050525	EP 2003-792402	20030821
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1688316	A	20051026	CN 2003-824405	20030821
CN 100502875	C	20090624		
JP 2006505527	T	20060216	JP 2004-530234	20030821
US 20050209219	A1	20050922	US 2005-524815	20050218
PRIORITY APPLN. INFO.:			DE 2002-10239531	A 20020823
			WO 2003-EP9254	W 20030821

AB The invention concerns the use of inhibitors of acid sphingomyelinase and/or of inhibitors of products (especially ceramide) catalyzed by reaction of this enzyme for prophylaxis and/or therapy of infectious diseases. Inhibitors include antibodies, especially neutralizing antibodies, and/or antidepressants, especially tricyclic and/or tetracyclic antidepressants.

IC ICM A61K039-395

CC 1-5 (Pharmacology)

Section cross-reference(s): 15

IT ~~50-48-6~~, Amitriptyline ~~50-49-7~~, Imipramine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(inhibitors of acid sphingomyelinase and of acid sphingomyelinase

reaction products for prophylaxis and treatment of infectious diseases)

IT ~~50-48-6~~, Amitriptyline ~~50-49-7~~, Imipramine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

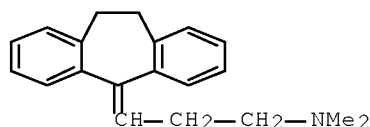
(inhibitors of acid sphingomyelinase and of acid sphingomyelinase

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reaction products for prophylaxis and treatment of infectious diseases)

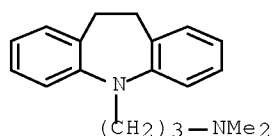
RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



RN 50-49-7 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



L89 ANSWER 21 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:171714 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:210564

TITLE: Detecting and influencing the expression or function of CD95/CD95L in infections

INVENTOR(S): Lang, Florian; Gulbins, Erich

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2002017950	A2	20020307	WO 2001-EP9889	20010828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042853	A1	20020425	DE 2000-10042853	20000830
AU 2002012170	A	20020313	AU 2002-12170	20010828

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PRIORITY APPLN. INFO.:

DE 2000-10042853 A 20000830  
WO 2001-EP9889 W 20010828

AB The invention discloses the use of a substance for detecting CD95 and/or CD95L, or members of the signal transduction cascade of CD95 and/or CD95L, in order to identify susceptibility to diseases that are related to an infection. The invention also discloses the use of an active substance for preventing and treating infections, in particular, bacterial infections, in which the active substance influences the expression and/or function of CD95 and/or CD95L, or members of the signal transduction cascade of CD95 and/or CD95L, thereby inducing apoptosis in the infected cells.

IC ICM A61K038-00

CC 1-7 (Pharmacology)

Section cross-reference(s): 9, 15

IT ~~CFTF~~ (cystic fibrosis transmembrane conductance regulator)

Fas antigen

Fas ligand

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CD95/CD95L detection and modulation in infections)

L89 ANSWER 22 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:623548 ZCAPLUS Full-text

DOCUMENT NUMBER: 133:187991

TITLE: Use of ceramides in the treatment of cystic fibrosis and other diseases associated with impaired membrane transport regulation

INVENTOR(S): Lang, Florian; Gulbins, Erich; Lepple-Wienhues, Albrecht

PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 8 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
DE 19909115	A1	20000907	DE 1999-19909115	19990303
CA 2365290	A1	20000908	CA 2000-2365290	20000229
WO 2000051578	A2	20000908	WO 2000-EP1682	20000229
WO 2000051578	A3	20010104		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1156854	A2	20011128	EP 2000-909267	20000229
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.:

DE 1999-19909115 A 19990303  
WO 2000-EP1682 W 20000229

AB The invention provides the use of ceramides (especially C2 and/or C6 ceramide), and/or substances which contain ceramides as components, for the treatment of cystic fibrosis. The invention also provides the use of the above-mentioned substances for the treatment of diseases which are associated with impaired regulation of membrane transport processes.

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IC ICM A61K031-16  
CC 1-12 (Pharmacology)  
Section cross-reference(s): 63  
ST C2 C6 ceramide **cystic fibrosis** treatment; membrane transport  
regulation disease treatment ceramide  
IT Biological transport  
Cystic fibrosis  
Drug delivery systems  
Membrane, biological  
T cell (lymphocyte)  
(ceramides for treatment of **cystic fibrosis** and  
other diseases associated with impaired membrane transport regulation)  
IT Ceramides  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(ceramides for treatment of **cystic fibrosis** and  
other diseases associated with impaired membrane transport regulation)  
IT Chloride channel  
Ion channel  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)  
(ceramides for treatment of **cystic fibrosis** and  
other diseases associated with impaired membrane transport regulation)  
IT 114051-78-4  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological  
process); BSU (Biological study, unclassified); BIOL (Biological study);  
PROC (Process)  
(ceramides for treatment of **cystic fibrosis** and  
other diseases associated with impaired membrane transport regulation)  
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)  
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 23 OF 37 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2009022109 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 19022708  
TITLE: Highlights of a workshop to discuss targeting inflammation  
in **cystic fibrosis**.  
AUTHOR: Banner Katharine H; De Jonge Hugo; Elborn Stuart; Growcott  
Ellena; Gulbins Erich; Konstan Mike; Moss Rick; Poll  
Chris; Randell Scott H; Rossi Adriano G; Thomas Lorraine;  
Waltz David  
CORPORATE SOURCE: Novartis Institutes for Biomedical Research, Wimblehurst  
Road, Horsham, West Sussex, RH12 5AB, UK..  
kathy.banner@novartis.com  
SOURCE: Journal of cystic fibrosis : official journal of the  
European Cystic Fibrosis Society, (2009 Jan) Vol. 8, No. 1,  
pp. 1-8. Electronic Publication: 2008-11-20. Ref: 78  
Journal code: 101128966. ISSN: 1569-1993.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200903

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ENTRY DATE: Entered STN: 2 Jan 2009  
Last Updated on STN: 11 Mar 2009  
Entered Medline: 10 Mar 2009

ABSTRACT:

A workshop to discuss anti-inflammatory approaches in the treatment of CF was held at Novartis Institutes for Biomedical Research (NIBR, Horsham, UK) in March 2008. Key opinion leaders in the field (Hugo De Jonge, Stuart Elborn, Erich Gulbins, Mike Konstan, Rick Moss, Scott Randell and Adriano Rossi), and NIBR scientists were brought together to collectively address three main aims: (i) to identify anti-inflammatory targets in CF, (ii) to evaluate the pros and cons of targeting specific cell types and (iii) to discuss model systems to profile potential therapeutic agents. The highlights of the workshop are captured in this review.

CONTROLLED TERM: Animals  
\*Anti-Inflammatory Agents: TU, therapeutic use  
Cystic Fibrosis: CO, complications  
\*Cystic Fibrosis: DT, drug therapy  
\*Cystic Fibrosis: PA, pathology  
Education  
Epithelial Cells: ME, metabolism  
Humans  
Inflammation: CO, complications  
\*Inflammation: DT, drug therapy  
\*Inflammation: PA, pathology  
Lymphocytes: ME, metabolism  
Models, Biological  
Neutrophils: ME, metabolism  
Research Design  
CHEMICAL NAME: 0 (Anti-Inflammatory Agents)

L89 ANSWER 24 OF 37 MEDLINE on STN DUPLICATE 19  
ACCESSION NUMBER: 2000420364 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 10930579  
TITLE: Acid sphingomyelinase is involved in CEACAM  
receptor-mediated phagocytosis of Neisseria gonorrhoeae.  
AUTHOR: Hauck C R; Grassme H; Bock J; Jendrosseck V; Ferlinz K;  
Meyer T F; Gulbins E  
CORPORATE SOURCE: Department of Physiology, University of Tübingen, Germany.  
SOURCE: FEBS letters, (2000 Aug 4) Vol. 478, No. 3, pp. 260-6.  
Journal code: 0155157. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200009  
ENTRY DATE: Entered STN: 15 Sep 2000  
Last Updated on STN: 22 Sep 2000  
Entered Medline: 7 Sep 2000

ABSTRACT:

The interaction with human phagocytes is a hallmark of symptomatic *Neisseria gonorrhoeae* infections. Gonococcal outer membrane proteins of the Opa family induce the opsonin-independent uptake of the bacteria that relies on CEACAM receptors and an active signaling machinery of the phagocyte. Here, we show that CEACAM receptor-mediated phagocytosis of Opa(52)-expressing *N. gonorrhoeae* into human cells results in a rapid activation of the acid sphingomyelinase. Inhibition of this enzyme by ~~imipramine~~ or SR33557 abolishes opsonin-independent internalization without affecting bacterial adherence. Reconstitution of ceramide, the product of acid sphingomyelinase activity, in ~~imipramine~~- or SR33557-treated cells restores internalization of the



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bacteria. Furthermore, we demonstrate that CEACAM receptor-initiated stimulation of other signalling molecules, in particular Src-like tyrosine kinases and Jun N-terminal kinases, requires acid sphingomyelinase. These studies provide evidence for a crucial role of the acid sphingomyelinase for CEACAM receptor-initiated signalling events and internalization of Opa(52)-expressing *N. gonorrhoeae* into human neutrophils.

CONTROLLED TERM:     Antigens, Bacterial: ME, metabolism  
                          Bacterial Adhesion: DE, drug effects  
                          Bacterial Outer Membrane Proteins: ME, metabolism  
                          \*Carcinoembryonic Antigen: ME, metabolism  
                          Cell Line  
                          Ceramides: PD, pharmacology  
                          Enzyme Activation  
                          Epithelial Cells: CY, cytology  
                          Epithelial Cells: DE, drug effects  
                          Epithelial Cells: EN, enzymology  
                          Epithelial Cells: MI, microbiology  
                          Humans  
                          Imipramine: PD, pharmacology  
                          Indolizines: PD, pharmacology  
                          Mitogen-Activated Protein Kinase 8  
                          Mitogen-Activated Protein Kinases: ME, metabolism  
                          Neisseria gonorrhoeae: IM, immunology  
                          \*Neisseria gonorrhoeae: ME, metabolism  
                          Phagocytes: DE, drug effects  
                          \*Phagocytes: EN, enzymology  
                          \*Phagocytes: IM, immunology  
                          Phagocytes: MI, microbiology  
                          \*Phagocytosis  
                          Phagocytosis: DE, drug effects  
                          Phenethylamines: PD, pharmacology  
                          Proto-Oncogene Proteins pp60(c-src): AI, antagonists &  
                          inhibitors  
                          Proto-Oncogene Proteins pp60(c-src): ME, metabolism  
                          \*Receptors, Cell Surface: ME, metabolism  
                          Signal Transduction: DE, drug effects  
                          Sphingomyelin Phosphodiesterase: AI, antagonists &  
                          inhibitors  
                          \*Sphingomyelin Phosphodiesterase: ME, metabolism  
CAS REGISTRY NO.:    114432-13-2 (fantofarone); 50-49-7 (Imipramine)  
CHEMICAL NAME:        0 (Antigens, Bacterial); 0 (Bacterial Outer Membrane  
                          Proteins); 0 (Carcinoembryonic Antigen); 0 (Ceramides); 0  
                          (Indolizines); 0 (Phenethylamines); 0 (Receptors, Cell  
                          Surface); 0 (opacity proteins); EC 2.7.1.112  
                          (Proto-Oncogene Proteins pp60(c-src)); EC 2.7.1.37  
                          (Mitogen-Activated Protein Kinase 8); EC 2.7.1.37  
                          (Mitogen-Activated Protein Kinases); EC 3.1.4.12  
                          (Sphingomyelin Phosphodiesterase)

L89   ANSWER 25 OF 37           MEDLINE on STN  
ACCESSION NUMBER:    2009071090       MEDLINE   Full-text  
DOCUMENT NUMBER:     PubMed ID: 19068098  
TITLE:                Cystic fibrosis and innate immunity: how chloride  
                          channel mutations provoke lung disease.  
AUTHOR:               Doring Gerd; Gulbins Erich  
CORPORATE SOURCE:     Institute of Medical Microbiology and Hygiene,  
                          Wilhelmstrasse 31, 72074 Tübingen, Germany..  
                          gerd.doering@med.uni-tuebingen.de  
SOURCE:               Cellular microbiology, (2009 Feb) Vol. 11, No. 2, pp.  
                          208-16.   Electronic Publication: 2008-12-02. Ref: 60

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Journal code: 100883691. E-ISSN: 1462-5822.  
PUB. COUNTRY: England; United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200902  
ENTRY DATE: Entered STN: 16 Jan 2009  
Last Updated on STN: 1 Mar 2009  
Entered Medline: 27 Feb 2009

ABSTRACT:

Innate immunity is essential for prevention of infection in vertebrates and plants and dysfunction of single components of innate immunity may provoke severe disease. Here we describe how mutations in the *cystic fibrosis* transmembrane conductance regulator gene dysregulate a variety of components of the innate immune system in individuals suffering from the hereditary disease *cystic fibrosis*. In the airways of these individuals, functions of the mucociliary clearance system, cationic antimicrobial (poly)peptides and neutrophils and macrophages are impaired and inflammatory signal transduction pathways exaggerated. Consequently, chronic airway colonization with opportunistic bacterial pathogens develops and leads to life-threatening lung disease.

CONTROLLED TERM: Animals  
\*Chloride Channels: GE, genetics  
\*Chloride Channels: IM, immunology  
\*Cystic Fibrosis: PA, pathology  
Humans  
\*Immunity, Innate  
\*Mutation  
CHEMICAL NAME: 0 (Chloride Channels)

L89 ANSWER 26 OF 37 MEDLINE on STN

ACCESSION NUMBER: 2009476152 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 19590194

TITLE: Therapeutic efficacy and safety of amitriptyline in patients with *cystic fibrosis*.

AUTHOR: Riethmuller Joachim; Anthonysamy Janina; Serra Emilio; Schwab Matthias; Doring Gerd; Gulbins Erich

CORPORATE SOURCE: Department of Paediatrics, University Hospital Tuebingen, Tuebingen, Germany..  
joachim.riethmueller@med.uni-tuebingen.de

SOURCE: Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology, (2009) Vol. 24, No. 1-2, pp. 65-72.  
Electronic Publication: 2009-07-01.  
Journal code: 9113221. E-ISSN: 1421-9778.

PUB. COUNTRY: Switzerland  
DOCUMENT TYPE: (CLINICAL TRIAL, PHASE II)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
(CLINICAL TRIAL)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200910  
ENTRY DATE: Entered STN: 11 Jul 2009  
Last Updated on STN: 6 Oct 2009  
Entered Medline: 5 Oct 2009

ABSTRACT:

Amitriptyline, a blocker of acid sphingomyelinase and acid ceramidase,

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significantly reduces *Pseudomonas aeruginosa* lung infection in cystic fibrosis (CF) mice with concurrent increase of survival. Our aim was to establish whether amitriptyline is safe and effective in the treatment of CF patients. In a randomised, double-blinded, placebo-controlled, cross-over pilot study, 4 adult CF patients received 37.5 mg of amitriptyline or placebo twice daily for 14 days. Subsequently in a phase II study 19 adult CF patients were randomly allocated to three treatment groups receiving amitriptyline once daily for 28 days at doses of 25 mg (n=7), 50 mg (n=8), or 75 mg (n=8) or placebo (n=13). The primary outcome was the difference of forced expiratory volume in 1 sec (FEV(1)) at day 14 between amitriptyline and placebo. Primary endpoint measures improved significantly in three of four patients in the pilot study after amitriptyline treatment vs placebo (relative FEV(1): 14.7+/-5%; p = 0.006) and in the 25 mg treatment group of the phase II study (relative FEV(1): 4.0+/-7%; p = 0.048). Amitriptyline was well tolerated in both studies and 96% of the patients completed the studies. Amitriptyline as a novel therapeutic option in patients with CF is safe and seems to be efficacious.

2009 S. Karger AG, Basel.

CONTROLLED TERM: Check Tags: Female; Male  
Adult  
Amitriptyline: AE, adverse effects  
\*Amitriptyline: TU, therapeutic use  
Anti-Bacterial Agents: AE, adverse effects  
\*Anti-Bacterial Agents: TU, therapeutic use  
\*Bacterial Infections: DT, drug therapy  
\*Cystic Fibrosis: DT, drug therapy  
Enzyme Inhibitors: AE, adverse effects  
\*Enzyme Inhibitors: TU, therapeutic use  
Forced Expiratory Volume  
Humans  
Pseudomonas Infections: DT, drug therapy  
Pseudomonas Infections: ET, etiology  
Treatment Outcome  
CAS REGISTRY NO.: 50-48-6 (Amitriptyline)  
CHEMICAL NAME: 0 (Anti-Bacterial Agents); 0 (Enzyme Inhibitors)

L89 ANSWER 27 OF 37 MEDLINE on STN  
ACCESSION NUMBER: 2008548021 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 18751925  
TITLE: Ceramide-enriched membrane domains in infectious biology and development.  
AUTHOR: Becker Katrin Anne; Gellhaus Alexandra; Winterhager Elke; Gulbins Erich  
CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany.  
SOURCE: Sub-cellular biochemistry, (2008) Vol. 49, pp. 523-38.  
Ref: 79  
Journal code: 0316571. ISSN: 0306-0225.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200812  
ENTRY DATE: Entered STN: 29 Aug 2008  
Last Updated on STN: 2 Jan 2009  
Entered Medline: 24 Dec 2008

ABSTRACT:  
Ceramide has been shown to be critically involved in multiple biological

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processes, for instance induction of apoptosis after ligation of death receptors or application of gamma-irradiation or UV-A light, respectively, regulation of cell differentiation, control of tumor cell growth, infection of mammalian cells with pathogenic bacteria and viruses or the control of embryo and organ development to name a few examples. Ceramide molecules form distinct large domains in the cell membrane, which may serve to re-organize cellular receptors and signalling molecules. Thus, in many conditions, ceramide may be involved in the spatial and temporal organisation of specific signalling pathways explaining the pleiotrophic effects of this lipid. Here, we focus on the role of ceramide and ceramide-enriched membrane domains, respectively, in bacterial infections, in particular of the lung, and sepsis. We describe the role of ceramide for infections with *Neisseriae gonorrhoeae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Finally, we discuss newly emerging aspects of the cellular function of ceramide, i.e. its role in germ line and embryo development.

CONTROLLED TERM:      Check Tags: Female; Male  
                         Animals  
                         Apoptosis: DE, drug effects  
                         \*Bacterial Infections: PP, physiopathology  
                         \*Cell Membrane: PH, physiology  
                         \*Ceramides: PH, physiology  
                         Cystic Fibrosis: PP, physiopathology  
                         Embryo Implantation: PH, physiology  
                         \*Embryonic Development: PH, physiology  
                         Germ Cells: GD, growth & development  
                         Gonorrhea: EN, enzymology  
                         Gonorrhea: ET, etiology  
                         Humans  
                         Parasitic Diseases: PP, physiopathology  
                         Pseudomonas Infections: ET, etiology  
                         Sepsis: EN, enzymology  
                         Sphingomyelin Phosphodiesterase: ME, metabolism  
                         Staphylococcal Infections: ET, etiology  
                         Virus Diseases: PP, physiopathology  
CHEMICAL NAME:        0 (Ceramides); EC 3.1.4.12 (Sphingomyelin  
                         Phosphodiesterase)

L89    ANSWER 28 OF 37            MEDLINE on STN  
ACCESSION NUMBER:    2005353059            MEDLINE    Full-text  
DOCUMENT NUMBER:    PubMed ID: 15888438  
TITLE:                Rhinoviruses infect human epithelial cells via  
                         ceramide-enriched membrane platforms.  
AUTHOR:               Grassme Heike; Riehle Andrea; Wilker Barbara; Gulbins Erich  
CORPORATE SOURCE:    Department of Molecular Biology, University of  
                         Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany.  
SOURCE:               The Journal of biological chemistry, (2005 Jul 15) Vol.  
                         280, No. 28, pp. 26256-62.    Electronic Publication:  
                         2005-05-10.  
                         Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY:        United States  
DOCUMENT TYPE:        Journal; Article; (JOURNAL ARTICLE)  
                         (RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE:            English  
FILE SEGMENT:        Priority Journals  
ENTRY MONTH:         200509  
ENTRY DATE:           Entered STN: 12 Jul 2005  
                         Last Updated on STN: 13 Sep 2005  
                         Entered Medline: 12 Sep 2005

ABSTRACT:  
The cell membrane contains very small distinct membrane domains enriched of

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sphingomyelin and cholesterol that are named rafts. We have shown that the formation of ceramide via activation of the acid sphingomyelinase transforms rafts into ceramide-enriched membrane platforms. These platforms are required for infection of mammalian cells with *Pseudomonas aeruginosa*, *Staphylococcus aureus*, or *Neisseriae gonorrhoeae*. In the present study we determined whether the acid sphingomyelinase, ceramide, and ceramide-enriched membrane platforms are also involved in the infection of human cells with pathogenic rhinoviruses. We demonstrate that infection of human epithelial cells with several rhinovirus strains triggers a rapid activation of the acid sphingomyelinase correlating with microtubules- and microfilament-mediated translocation of the enzyme from an intracellular compartment onto the extracellular leaflet of the cell membrane. The activity of the acid sphingomyelinase results in the formation of ceramide in the cell membrane and, finally, large ceramide-enriched membrane platforms. Rhinoviruses colocalize with ceramide-enriched membrane platforms during the infection. The significance of ceramide-enriched membrane platforms for rhinoviral uptake is demonstrated by the finding that genetic deficiency or pharmacological inhibition of the acid sphingomyelinase prevented infection of human epithelial cells by rhinoviruses. The data identify the acid sphingomyelinase and ceramide as key molecules for the infection of human cells with rhinoviruses.

CONTROLLED TERM:      Adrenergic Uptake Inhibitors: PD, pharmacology  
                          Amitriptyline: PD, pharmacology  
                          Annexins: PD, pharmacology  
                          Cell Line  
                          \*Cell Membrane: ME, metabolism  
                          Ceramides: ME, metabolism  
                          \*Ceramides: PD, pharmacology  
                          Diacylglycerol Kinase: ME, metabolism  
                          Enzyme Activation  
                          Enzyme Inhibitors: PD, pharmacology  
                          \*Epithelial Cells: ME, metabolism  
                          Epithelial Cells: VI, virology  
                          Fibroblasts: ME, metabolism  
                          Hela Cells  
                          Humans  
                          Imipramine: PD, pharmacology  
                          Membrane Microdomains: CH, chemistry  
                          Microfilaments: ME, metabolism  
                          Microscopy, Confocal  
                          Microscopy, Fluorescence  
                          Microtubules: ME, metabolism  
                          Neisseria gonorrhoeae: ME, metabolism  
                          Protein Transport  
                          Pseudomonas aeruginosa: ME, metabolism  
                          \*Rhinovirus: ME, metabolism  
                          Sphingomyelin Phosphodiesterase: CH, chemistry  
                          Sphingomyelin Phosphodiesterase: GE, genetics  
                          Sphingomyelins: CH, chemistry  
                          Sphingomyelins: ME, metabolism  
                          Staphylococcus aureus: ME, metabolism  
                          Time Factors  
CAS REGISTRY NO.:    50-48-6 (Amitriptyline); 50-49-7 (Imipramine)  
CHEMICAL NAME:        0 (Adrenergic Uptake Inhibitors); 0 (Annexins); 0  
                          (Ceramides); 0 (Enzyme Inhibitors); 0 (Sphingomyelins); EC  
                          2.7.1.107 (Diacylglycerol Kinase); EC 3.1.4.- (acid  
                          sphingomyelinase-1); EC 3.1.4.12 (Sphingomyelin  
                          Phosphodiesterase)

L89    ANSWER 29 OF 37      MEDLINE on STN  
ACCESSION NUMBER:    1999218554      MEDLINE    Full-text

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DOCUMENT NUMBER: PubMed ID: 10200443  
TITLE: Fas/CD95/Apo-I activates the acidic sphingomyelinase via caspases.  
AUTHOR: Brenner B; Ferlinz K; Grassme H; Weller M; Koppenhoefer U; Dichgans J; Sandhoff K; Lang F; Gulbins E  
CORPORATE SOURCE: Department of Physiology, University of Tuebingen, Gmelinstrasse 5, 72076 Tuebingen, Germany.  
SOURCE: Cell death and differentiation, (1998 Jan) Vol. 5, No. 1, pp. 29-37.  
Journal code: 9437445. ISSN: 1350-9047.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199904  
ENTRY DATE: Entered STN: 17 May 1999  
Last Updated on STN: 17 May 1999  
Entered Medline: 30 Apr 1999

ABSTRACT:

Fas/CD95/Apo-I has been shown to stimulate a variety of molecules including several members of the caspase family and the acidic sphingomyelinase (Martin and Green 1995; Gulbins et al, 1995). Here, we demonstrate that Fas receptor-triggered activation of the acidic sphingomyelinase, consumption of sphingomyelin, release of ceramide, and subsequent activation of JNK and p38-K are regulated by caspases. Inhibition of caspases by Ac-YVAD-chloromethylketone or transient CrmA transfection prevented stimulation of acidic sphingomyelinase, release of ceramide and activation of JNK and p38-K upon Fas-receptor crosslinking. Likewise, Fas triggered apoptosis was almost completely blocked by Ac-YVAD-chloromethylketone or CrmA mediated inhibition of caspases. The results suggest a new signalling cascade from the Fas receptor via caspases to acidic sphingomyelinase, ceramide and JNK/p38-K.

CONTROLLED TERM: Acids: ME, metabolism  
Adrenergic Uptake Inhibitors: PD, pharmacology  
Amino Acid Chloromethyl Ketones: PD, pharmacology  
\*Antigens, CD95: ME, metabolism  
Apoptosis: DE, drug effects  
\*Apoptosis: PH, physiology  
Calcium-Calmodulin-Dependent Protein Kinases: ME, metabolism  
\*Caspases: ME, metabolism  
Ceramides: ME, metabolism  
Cysteine Proteinase Inhibitors: GE, genetics  
Cysteine Proteinase Inhibitors: PD, pharmacology  
Diglycerides: ME, metabolism  
Gene Expression Regulation, Enzymologic  
Humans  
Imipramine: PD, pharmacology  
\*Jurkat Cells: CY, cytology  
Jurkat Cells: EN, enzymology  
\*Mitogen-Activated Protein Kinases  
Serpins: GE, genetics  
Signal Transduction: PH, physiology  
\*Sphingomyelin Phosphodiesterase: ME, metabolism  
T-Lymphocytes: CY, cytology  
T-Lymphocytes: EN, enzymology  
Transfection  
\*Viral Proteins  
p38 Mitogen-Activated Protein Kinases  
CAS REGISTRY NO.: 50-49-7 (Imipramine); 96282-35-8

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CHEMICAL NAME: (interleukin-1beta-converting enzyme inhibitor)  
0 (Acids); 0 (Adrenergic Uptake Inhibitors); 0 (Amino Acid Chloromethyl Ketones); 0 (Antigens, CD95); 0 (Ceramides); 0 (Cysteine Proteinase Inhibitors); 0 (Diglycerides); 0 (N-acetyl-tyrosyl-valyl-alanyl-aspartyl chloromethyl ketone); 0 (Serpins); 0 (Viral Proteins); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (p38 Mitogen-Activated Protein Kinases); EC 2.7.11.17 (Calcium-Calmodulin-Dependent Protein Kinases); EC 3.1.4.12 (Sphingomyelin Phosphodiesterase); EC 3.4.22.- (Caspases)

L89 ANSWER 30 OF 37 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007054516 EMBASE Full-text  
TITLE: The cold case: Are rhinoviruses perfectly adapted pathogens?.  
AUTHOR: Dreschers, S. (correspondence); Dumitru, C.A.; Adams, C.; Gulbins, E.  
CORPORATE SOURCE: Dept. of Molecular Biology, University of Duisburg-Essen, Hufelandstr. 55, 45122 Essen, Germany. stephan.dreschers@uni-essen.de  
SOURCE: Cellular and Molecular Life Sciences, (Jan 2007) Vol. 64, No. 2, pp. 181-191.  
Refs: 88  
ISSN: 1420-682X; E-ISSN: 1569-1632 CODEN: CMLSFI  
COUNTRY: Switzerland  
DOCUMENT TYPE: Journal; General Review; (Review)  
FILE SEGMENT: 011 Otorhinolaryngology  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 14 Feb 2007  
Last Updated on STN: 14 Feb 2007

ABSTRACT: Rhinoviruses, which cause common cold, belong to the Picornaviridae family, small non-enveloped viruses (diameter 15-30 nm) containing a single-stranded RNA genome (about 7 kb). Over 100 different rhinoviral serotypes have been identified thus far, establishing rhinoviruses as the most diverse group of Picomaviridae. Based on receptor binding properties, rhinoviruses are divided into two classes: the major group binding to intracellular adhesion molecule-1 and the minor group binding to the very low density lipoprotein receptors. Interactions between virus and the receptor molecules cause a conformational change in the capsid, which is a prerequisite for viral uptake. Rhinoviruses trigger a chemokine response upon infection that may lead to exacerbation of the symptoms of common cold, i.e. asthma and inflammation. The following review aims to summarize the knowledge about rhinoviral infections and discusses therapeutical approaches against this almost perfectly adapted pathogen. .COPYRGT. Birkhauser Verlag, 2007.

CONTROLLED TERM: Medical Descriptors:  
absence of side effects: SI, side effect  
asthma  
chronic obstructive lung disease  
clinical feature  
\*common cold: DT, drug therapy  
\*common cold: ET, etiology  
disease exacerbation

drug megadose  
 electron microscopy  
 human  
 internalization  
 lipid composition  
 nonhuman  
 nose congestion: SI, side effect  
 nose injury: SI, side effect  
 open reading frame  
 protein family  
 protein structure  
 review  
 \*Rhinovirus  
 signal transduction  
 upper respiratory tract infection: ET, etiology  
 virion  
 virus capsid  
 virus classification  
 virus detection  
 virus envelope  
 virus identification  
 virus morphogenesis  
 virus morphology  
 virus strain  
 virus transmission  
 virus virulence  
 X ray crystallography

## CONTROLLED TERM:

Drug Descriptors:  
 amitriptyline: PD, pharmacology  
 disoxaril: PD, pharmacology  
 imipramine: PD, pharmacology  
 intercellular adhesion molecule 1: EC, endogenous compound  
 interferon: AE, adverse drug reaction  
 interferon: DO, drug dose  
 interferon: DT, drug therapy  
 interferon: NA, intranasal drug administration  
 interleukin 8: EC, endogenous compound  
 low density lipoprotein receptor: EC, endogenous compound  
 rupintrivir: AE, adverse drug reaction  
 rupintrivir: DT, drug therapy  
 vascular cell adhesion molecule 1: EC, endogenous compound  
 virus receptor: EC, endogenous compound

## CAS REGISTRY NO.:

(amitriptyline) 50-48-6, 549-18-8; (disoxaril)  
 87495-31-6; (imipramine) 113-52-0, 50-49-7;  
 (intercellular adhesion molecule 1) 126547-89-5;  
 (interleukin 8) 114308-91-7; (rupintrivir) 223537-30-2

## CHEMICAL NAME:

ag7088; win 51711

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ACCESSION NUMBER: 2007085532 EMBASE Full-text

TITLE: Liver cell death and anemia in Wilson disease involve acid sphingomyelinase and ceramide.

AUTHOR: Lang, Philipp A.; Nicolay, Jan P.; Kempe, Daniela S.;  
 Lupescu, Adrian; Koka, Saisudha; Eisele, Kerstin; Klarl,  
 Barbara A.; Huber, Stephan M.; Wieder, Thomas; Lang,  
 Florian

CORPORATE SOURCE: Institute of Physiology, University of Tübingen, 72076  
 Tübingen, Germany. florian.lang@uni-tuebingen.de

AUTHOR: Schenck, Marcus; Gulbins, Erich (correspondence)



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CORPORATE SOURCE: Institute of Molecular Biology, University of  
Duisburg-Essen, 45122 Essen, Germany. erich.gulbins@uni-due  
.de

AUTHOR: Schenck, Marcus; Rubben, Herbert

CORPORATE SOURCE: Department of Urology, University of Duisburg-Essen, 45122  
Essen, Germany.

AUTHOR: Becker, Jan Ulrich; Schmid, Kurt W.

CORPORATE SOURCE: Institute of Pathology and Neuropathology, University of  
Duisburg-Essen, 45122 Essen, Germany.

AUTHOR: Mann, Klaus

CORPORATE SOURCE: Department of Internal Medicine, University Clinic,  
University of Duisburg-Essen, 45122 Essen, Germany.

AUTHOR: Hildenbrand, Sibylle

CORPORATE SOURCE: Department of Occupational and Social Medicine, University  
of Tübingen, 72076 Tübingen, Germany.

AUTHOR: Hefter, Harald

CORPORATE SOURCE: Department of Neurology, University of Düsseldorf, 40225  
Düsseldorf, Germany.

AUTHOR: Erhardt, Andreas; Haussinger, Dieter

CORPORATE SOURCE: Department of Gastroenterology, Hepatology and  
Infectiology, University of Düsseldorf, 40225 Düsseldorf,  
Germany.

AUTHOR: Wieder, Thomas

CORPORATE SOURCE: Department of Dermatology, University of Tübingen, 72076  
Tübingen, Germany.

SOURCE: Nature Medicine, (Feb 2007) Vol. 13, No. 2, pp. 164-170.  
Refs: 45  
ISSN: 1078-8956; E-ISSN: 1546-170X CODEN: NAMEFI

PUBLISHER IDENT.: NM1539

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 025 Hematology  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index  
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Mar 2007  
Last Updated on STN: 14 Mar 2007

ABSTRACT: Wilson disease is caused by accumulation of Cu<sup>2+</sup> in cells, which  
results in liver cirrhosis and, occasionally, anemia. Here, we show that Cu<sup>2+</sup>  
triggers hepatocyte apoptosis through activation of acid sphingomyelinase (Asm)  
and release of ceramide. Genetic deficiency or pharmacological inhibition of  
Asm prevented Cu<sup>2+</sup>-induced hepatocyte apoptosis and protected rats, genetically  
prone to develop Wilson disease, from acute hepatocyte death, liver failure and  
early death. Cu<sup>2+</sup> induced the secretion of activated Asm from leukocytes,  
leading to ceramide release in and phosphatidylserine exposure on erythrocytes,  
events also prevented by inhibition of Asm. Phosphatidylserine exposure  
resulted in immediate clearance of affected erythrocytes from the blood in  
mice. Accordingly, individuals with Wilson disease showed elevated plasma  
levels of Asm, and displayed a constitutive increase of ceramide- and  
phosphatidylserine-positive erythrocytes. Our data suggest a previously  
unidentified mechanism for liver cirrhosis and anemia in Wilson disease.  
.COPYRG. 2007 Nature Publishing Group.

CONTROLLED TERM: Medical Descriptors:  
adult  
\*anemia  
animal cell  
apoptosis

article  
 blood level  
 \*cell death  
 controlled study  
 drug activation  
 drug inhibition  
 erythrocyte  
 female  
 human  
 leukocyte  
 liver cell  
 liver cirrhosis  
 liver failure  
 mouse  
 nonhuman  
 priority journal  
 protein deficiency: DT, drug therapy  
 \*Wilson disease: DT, drug therapy  
 Drug Descriptors:  
 amitriptyline: DT, drug therapy  
 amitriptyline: IP, intraperitoneal drug administration  
 \*ceramide

## CONTROLLED TERM:

copper  
 penicillamine: DT, drug therapy  
 phosphatidylserine  
 \*sphingomyelin phosphodiesterase: PD, pharmacology  
 trientine: DT, drug therapy

## CAS REGISTRY NO.:

(amitriptyline) 50-48-6, 549-18-8; (copper)  
 15158-11-9, 7440-50-8; (penicillamine) 2219-30-9, 52-67-5;  
 (sphingomyelin phosphodiesterase) 9031-54-3; (trientine)  
 112-24-3, 38260-01-4

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ACCESSION NUMBER: 2000418614 EMBASE Full-text

TITLE: Physiology of apoptosis.

AUTHOR: Gulbins, E. (correspondence); Jekle, A.; Ferlinz, K.;  
 Grassme, H.; Lang, F.

CORPORATE SOURCE: Dept. of Physiology, Univ. of Tuebingen, Gmelinstrasse 5,  
 72076 Tuebingen, Germany. erich.gulbins@uni-tuebingen.de

SOURCE: American Journal of Physiology - Renal Physiology, (2000)  
 Vol. 279, No. 4 48-4, pp. F605-F615.

Refs: 113

ISSN: 0363-6127 CODEN: AJPPFK

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 005 General Pathology and Pathological Anatomy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Dec 2000

Last Updated on STN: 14 Dec 2000

ABSTRACT: Ion fluxes and volume changes of the whole cell as well as of  
 organelles belong to the hallmarks of apoptosis; however, the molecular  
 mechanism regulating these changes is only poorly characterized. Several ion  
 channels in the plasma membrane, in particular the N-type K<sup>+</sup> channel, the  
 chloride channel *cystic fibrosis* conductance regulator, and an outward  
 rectifying chloride channel, as well as the mitochondrial permeability  
 transition pore, have been implicated to be involved in signal transduction  
 cascades regulating apoptosis. Furthermore, Bcl-2-like proteins have been  
 suggested to function, at least in part, as ion channels, because they display

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some homology to bacterial pore-forming toxins. In contrast to the demonstration of the involvement of these different ion channels in apoptosis, the molecular consequences regulated by these ion channels, and finally triggering apoptosis, are almost completely unknown.

CONTROLLED TERM: Medical Descriptors:

\*apoptosis  
molecular biology  
priority journal  
review  
signal transduction

CONTROLLED TERM: Drug Descriptors:

ceramide: EC, endogenous compound  
potassium channel  
protein bcl 2: EC, endogenous compound  
sodium channel  
sphingomyelin: EC, endogenous compound  
transmembrane conductance regulator: EC, endogenous compound

CAS REGISTRY NO.: (protein bcl 2) 219306-68-0; (sphingomyelin) 85187-10-6

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ACCESSION NUMBER: 2009:215509 BIOSIS Full-text

DOCUMENT NUMBER: PREV200900215509

TITLE: Ceramide-Enriched Membrane Domains in Infectious Biology and Development.

AUTHOR(S): Becker, Katrin Anne [Reprint Author]; Gellhaus, Alexandra; Winterhager, Elke; Gulbins, Erich

CORPORATE SOURCE: Univ Duisburg Essen, Dept Mol Biol, Hufelandstr 55, D-45122 Essen, Germany

SOURCE: Quinn, PJ [Editor]; Wang, X [Editor]. Subcellular Biochemistry, (2008) pp. 523-538. Subcellular Biochemistry. Publisher: SPRINGER, 233 SPRING STREET, NEW YORK, NY 10013, UNITED STATES. Series: SUBCELLULAR BIOCHEMISTRY. ISSN: 0306-0225. ISBN: 978-1-4020-8830-8(H).

DOCUMENT TYPE: Book; (Book Chapter)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Mar 2009

Last Updated on STN: 25 Mar 2009

ABSTRACT: Ceramide has been shown to be critically involved in multiple biological processes, for instance induction of apoptosis after ligation of death receptors or application of gamma-irradiation or UV-A light, respectively, regulation of cell differentiation, control of tumor cell growth, infection of mammalian cells with pathogenic bacteria and viruses or the control of embryo and organ development to name a few examples. Ceramide molecules form distinct large domains in the cell membrane, which may serve to re-organize cellular receptors and signalling molecules. Thus, in many conditions, ceramide may be involved in the spatial and temporal organisation of specific signalling pathways explaining the pleiotrophic effects of this lipid. Here, we focus on the role of ceramide and ceramide-enriched membrane domains, respectively, in bacterial infections, in particular of the lung, and sepsis. We describe the role of ceramide for infections with *Neisseriae gonorrhoeae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Finally, we discuss newly emerging aspects of the cellular function of ceramide, i.e. its role in germ line and embryo development.

CONCEPT CODE: Genetics - Animal 03506  
Biochemistry studies - General 10060  
Biochemistry studies - Lipids 10066  
Digestive system - Pathology 14006

Respiratory system - Physiology and biochemistry 16004  
 Respiratory system - Pathology 16006  
 Development and Embryology - Pathology 25503  
 Physiology and biochemistry of bacteria 31000  
 Virology - General and methods 33502  
 Medical and clinical microbiology - General and methods 36001  
 Medical and clinical microbiology - Bacteriology 36002  
 INDEX TERMS: Major Concepts  
                   Biochemistry and Molecular Biophysics; Infection  
 INDEX TERMS: Parts, Structures, & Systems of Organisms  
                   lung: respiratory system; cell membrane  
 INDEX TERMS: Diseases  
                   bacterial infection: bacterial disease  
                   Bacterial Infections (MeSH)  
 INDEX TERMS: Diseases  
                   sepsis: infectious disease  
                   Sepsis (MeSH)  
 INDEX TERMS: Diseases  
                   cystic fibrosis: respiratory system disease, genetic  
                   disease, congenital disease, digestive system disease  
                   Cystic Fibrosis (MeSH)  
 INDEX TERMS: Chemicals & Biochemicals  
                   ceramide; death receptors; ceramide-enriched membrane  
                   domains  
 INDEX TERMS: Methods & Equipment  
                   gamma-irradiation: therapeutic and prophylactic  
                   techniques, clinical techniques; UV-A light: laboratory  
                   techniques, spectrum analysis techniques  
 INDEX TERMS: Miscellaneous Descriptors  
                   apoptosis; cell differentiation; cell growth; organ  
                   development; embryo development  
 ORGANISM: Classifier  
                   Mammalia 85700  
                   Super Taxa  
                   Vertebrata; Chordata; Animalia  
                   Organism Name  
                   mammal (common)  
                   Taxa Notes  
                   Animals, Chordates, Mammals, Nonhuman Vertebrates,  
                   Nonhuman Mammals, Vertebrates  
 ORGANISM: Classifier  
                   Micrococcaceae 07702  
                   Super Taxa  
                   Gram-Positive Cocci; Eubacteria; Bacteria;  
                   Microorganisms  
                   Organism Name  
                   Staphylococcus aureus (species): pathogen  
                   Taxa Notes  
                   Bacteria, Eubacteria, Microorganisms  
 ORGANISM: Classifier  
                   Neisseriaceae 06507  
                   Super Taxa  
                   Gram-Negative Aerobic Rods and Cocci; Eubacteria;  
                   Bacteria; Microorganisms  
                   Organism Name  
                   Neisseria gonorrhoeae (species): pathogen  
                   Taxa Notes  
                   Bacteria, Eubacteria, Microorganisms  
 ORGANISM: Classifier

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Viruses 03000  
Super Taxa  
Microorganisms  
Organism Name  
Virus (common): pathogen  
Taxa Notes  
Microorganisms, Viruses

REGISTRY NUMBER: 104404-17-3 (ceramide)

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ACCESSION NUMBER: 2004:111812 BIOSIS Full-text

DOCUMENT NUMBER: PREV200400114499

TITLE: Role and biophysics of ceramide in bacterial and viral  
infections.

AUTHOR(S): Gulbins, Erich [Reprint Author]

CORPORATE SOURCE: Dept. of Molecular Biology, University of Duisburg-Essen,  
Essen, Germany

SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp.  
194a. print.

Meeting Info.: 48th Annual Meeting of the Biophysical  
Society. Baltimore, MD, USA. February 14-18, 2004.

Biophysical Society.

ISSN: 0006-3495 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Feb 2004

Last Updated on STN: 25 Feb 2004

ABSTRACT: We have recently shown that infection of mammalian lung epithelial cells with *P. aeruginosa* results in an activation of the acid sphingomyelinase (ASM) and a translocation of the enzyme onto the extracellular leaflet of the cell membrane. The activity of the ASM triggers the release of ceramide that reorganizes small membrane rafts to larger platforms. Ceramide enriched membrane platforms serve to cluster receptor molecules, e.g. ~~CFTN~~ and CD95, that mediate infection with *P. aeruginosa*. Here, we show that a very similar concept applies to infection of epithelial cells with human rhinovirus and *Salmonella typhimurium*. Rhinovirus induces an activation of the ASM and the formation of very large ceramide-enriched membrane platforms that co-localize with colera-toxin suggesting that they are formed by the fusion of small membrane rafts. These ceramide-enriched membrane platforms are required for the infection with rhinovirus since destruction of membrane rafts or inhibition of the ASM prevents viral uptake and, thus, infection. Likewise, *S. typhimurium* is internalized via ceramide-enriched membrane platforms that are formed by activation of the ASM. In addition, the fusion of the intracellular phagosome containing *S. typhimurium* with phagosomes to form a phagolysosome also requires activity of the acid sphingomyelinase and release of ceramide in the vesicle membrane. Similar data were obtained with BCG mycobacteria. The fusion of intracellular phagosomes that contain the bacteria with lysosomes requires ASM activity and formation of ceramide, while the uptake of BCG seems to be independent of ASM. Thus, ceramide-enriched membrane domains serve as "entrance gates" for several pathogens and, in addition, are critically involved in the fusion of phagosomes with lysosomes.

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520

Cytology - General 02502

Biochemistry studies - General 10060

Biochemistry studies - Lipids 10066

Enzymes - General and comparative studies: coenzymes  
10802

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Morphology and cytology of bacteria 30500  
Physiology and biochemistry of bacteria 31000  
Virology - General and methods 33502  
Medical and clinical microbiology - Virology 36006

INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Cell Biology;  
Infection

INDEX TERMS: Parts, Structures, & Systems of Organisms  
intracellular phagosomes, fusion; lysosomes; phagosome

INDEX TERMS: Diseases  
bacterial infection: bacterial disease  
Bacterial Infections (MeSH)

INDEX TERMS: Diseases  
viral infection: viral disease  
Virus Diseases (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
acid sphingomyelinase [EC 3.1.4.12]: activation;  
ceramide: formation

ORGANISM: Classifier  
Enterobacteriaceae 06702  
Super Taxa  
Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
Salmonella typhimurium (species)  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
Picornaviridae 03603  
Super Taxa  
Positive Sense ssRNA Viruses; Viruses; Microorganisms  
Organism Name  
Rhinovirus (genus): pathogen  
Taxa Notes  
Microorganisms, Positive Sense Single-Stranded RNA  
Viruses, Viruses

ORGANISM: Classifier  
Pseudomonadaceae 06508  
Super Taxa  
Gram-Negative Aerobic Rods and Cocci; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
Pseudomonas aeruginosa (species): pathogen  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 9031-54-3 (acid sphingomyelinase)  
9031-54-3 (EC 3.1.4.12)  
104404-17-3 (ceramide)

L89 ANSWER 35 OF 37 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on  
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ACCESSION NUMBER: 2002:362613 BIOSIS Full-text  
DOCUMENT NUMBER: PREV200200362613  
TITLE: P. aeruginosa infects mammalian cells via membrane rafts.  
AUTHOR(S): Gulbins, E. [Reprint author]; Grassme, H. [Reprint author]  
CORPORATE SOURCE: Dept. of Molecular Biology, University of Essen,  
Hufelandstrasse 55, 45122, Essen, Germany  
SOURCE: Pfluegers Archiv European Journal of Physiology, (March,  
2002) Vol. 443, No. Supplement 1, pp. S161-S162. print.  
Meeting Info.: 81st Annual Joint Meeting of the

10/524815

Physiological Society, the Scandinavian Physiological Society and the German Physiological Society. Tuebingen, Germany. March 15-19, 2002.  
CODEN: PFLABK. ISSN: 0031-6768.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Jul 2002  
Last Updated on STN: 3 Jul 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520  
Cytology - Animal 02506  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Biophysics - Membrane phenomena 10508  
Pathology - General 12502  
Morphology and cytology of bacteria 30500  
Physiology and biochemistry of bacteria 31000  
Medical and clinical microbiology - Bacteriology 36002  
Invertebrata: comparative, experimental morphology, physiology and pathology - Aschelminthes 64016

INDEX TERMS: Major Concepts  
Infection; Membranes (Cell Biology)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
cell surface; membrane raft

INDEX TERMS: Diseases  
P. aeruginosa infection: bacterial disease, pathology, Pseudomonas aeruginosa infection  
Pseudomonas Infections (MeSH)

INDEX TERMS: Diseases  
S. typhimurium infection: bacterial disease, pathology, Salmonella typhimurium infection  
Salmonella Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
CD95; CD95 ligand; CD95 receptor; cystic fibrosis conductance regulator

INDEX TERMS: Miscellaneous Descriptors  
functional type III secretion system: modulation; Meeting Abstract

ORGANISM: Classifier  
Enterobacteriaceae 06702  
Super Taxa  
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms  
Organism Name  
S. typhimurium [Salmonella typhimurium]: pathogen  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
Mammalia 85700  
Super Taxa  
Vertebrata; Chordata; Animalia  
Organism Name  
mammal  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGANISM: Classifier  
Nematoda 51300  
Super Taxa

Aschelminthes; Helminthes; Invertebrata; Animalia  
 Organism Name  
 Caenorhabditis elegans [worm]: host  
 Taxa Notes  
 Animals, Aschelminths, Helminths, Invertebrates  
 Classifier  
 Pseudomonadaceae 06508  
 Super Taxa  
 Gram-Negative Aerobic Rods and Cocci; Eubacteria;  
 Bacteria; Microorganisms  
 Organism Name  
 P. aeruginosa [Pseudomonas aeruginosa]: pathogen  
 Taxa Notes  
 Bacteria, Eubacteria, Microorganisms  
 REGISTRY NUMBER: 81271-93-4 (CD95)  
 GENE NAME: Caenorhabditis elegans ced 3 gene (Nematoda): activation,  
 regulation; Caenorhabditis elegans ced 4 gene (Nematoda):  
 activation, regulation

L89 ANSWER 36 OF 37 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on  
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ACCESSION NUMBER: 2002:596410 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200200596410  
 TITLE: Molecular mechanisms of pulmonary P. aeruginosa infections.  
 AUTHOR(S): Gulbins, M. [Reprint author]; Grassme, H. [Reprint author]  
 CORPORATE SOURCE: Dept. of Molecular Biology, University of Essen,  
 Hufelandstrasse 55, 45122, Essen, Germany  
 SOURCE: International Journal of Molecular Medicine, (2002) Vol.  
 10, No. Supplement 1, pp. S95. print.  
 Meeting Info.: 7th World Congress on Advances in Oncology  
 and the 5th International Symposium on Molecular Medicine.  
 Hersonissos, Crete, Greece. October 10-12, 2002.  
 ISSN: 1107-3756.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 20 Nov 2002  
 Last Updated on STN: 20 Nov 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
 00520  
 Cytology - Animal 02506  
 Cytology - Human 02508  
 Genetics - Human 03508  
 Biochemistry studies - Proteins, peptides and amino acids  
 10064  
 Biochemistry studies - Lipids 10066  
 Enzymes - General and comparative studies: coenzymes  
 10802  
 Metabolism - Metabolic disorders 13020  
 Digestive system - Pathology 14006  
 Respiratory system - Physiology and biochemistry 16004  
 Respiratory system - Pathology 16006  
 Physiology and biochemistry of bacteria 31000  
 Medical and clinical microbiology - Bacteriology 36002

INDEX TERMS: Major Concepts  
 Infection; Respiratory System (Respiration)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
 lung epithelial cells: respiratory system, apoptosis

INDEX TERMS: Diseases  
 cystic fibrosis: digestive system disease, genetic



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disease, metabolic disease, respiratory system disease  
**Cystic Fibrosis** (MeSH)

INDEX TERMS: Diseases  
pulmonary *Pseudomonas aeruginosa* infection: bacterial  
disease, respiratory system disease, etiology  
*Pseudomonas* Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
CD95; CD95 ligand; acid sphingomyelinase; ceramide

INDEX TERMS: Miscellaneous Descriptors  
molecular mechanisms; Meeting Abstract

ORGANISM: Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates,  
Vertebrates

ORGANISM: Classifier  
*Pseudomonadaceae* 06508  
Super Taxa  
Gram-Negative Aerobic Rods and Cocci; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
*P. aeruginosa* [*Pseudomonas aeruginosa*]: pathogen  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 81271-93-4 (CD95)  
9031-54-3 (acid sphingomyelinase)  
104404-17-3 (ceramide)

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ACCESSION NUMBER: 2001:248593 BIOSIS Full-text

DOCUMENT NUMBER: PREV200100248593

TITLE: Involvement of mitochondria and stress activated kinases in  
*P. aeruginosa* induced apoptosis.

AUTHOR(S): Jendrossek, V. [Reprint author]; Grassme, H.; Mueller, I.;  
Lang, F.; Gulbins, E.

CORPORATE SOURCE: Dept. of Physiology, University of Tuebingen, Gmelinstrasse  
5, 72076, Tuebingen, Germany

SOURCE: Pfluegers Archiv European Journal of Physiology, (2001)  
Vol. 441, No. 6 Supplement, pp. R141. print.  
Meeting Info.: Joint Congress of the Scandinavian and the  
German Physiological Societies. Berlin, Germany. March  
10-13, 2001.  
CODEN: PFLABK. ISSN: 0031-6768.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 23 May 2001  
Last Updated on STN: 19 Feb 2002

CONCEPT CODE: Medical and clinical microbiology - Bacteriology 36002  
General biology - Symposia, transactions and proceedings  
00520  
Cytology - General 02502  
Cytology - Human 02508  
Enzymes - General and comparative studies: coenzymes  
10802

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Morphology and cytology of bacteria 30500  
Physiology and biochemistry of bacteria 31000

INDEX TERMS: Major Concepts  
Enzymology (Biochemistry and Molecular Biophysics); Cell  
Biology; Infection

INDEX TERMS: Parts, Structures, & Systems of Organisms  
mitochondria

INDEX TERMS: Diseases  
Pseudomonas aeruginosa infection: bacterial disease  
Pseudomonas Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
Jun N-terminal kinases: activation; **cystic fibrosis**  
conductance regulator; cytochrome c: release; reactive  
oxygen intermediates: synthesis; stress activated  
kinases

INDEX TERMS: Miscellaneous Descriptors  
apoptosis; cellular depolarization; cellular signaling;  
immunocompromization; Meeting Abstract

ORGANISM: Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
Chang cell line: human conjunctiva epithelial cells  
human: patient  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates,  
Vertebrates

ORGANISM: Classifier  
Pseudomonadaceae 06508  
Super Taxa  
Gram-Negative Aerobic Rods and Cocci; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
Pseudomonas aeruginosa: pathogen, strain-PAO-I  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 9007-43-6 (cytochrome c)

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=> file registry

FILE 'REGISTRY' ENTERED AT 11:26:43 ON 14 OCT 2009  
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DICTIONARY FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6

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FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

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reclassification data for the third quarter of 2009.

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This file contains CAS Registry Numbers for easy and accurate  
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=> d stat que L32

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L23      36339 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ANTIDEPRESSANT?/BI OR
          ANTI DEPRESSANT?/BI
L24      15309 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ?CYSTIC FIBROS?/BI
L25        609 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROCYSTIC?/BI OR
          FIBRO CYSTIC?/BI
L26        155 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  MUCOVISCIDOSIS/BI
L27        5892 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  CFTR/BI
L28      15430 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROSIS/BI (L)
          CYSTIC/BI
L29      16341 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR
          L27 OR L28)
L32        9 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L23 AND (TRICYCLIC?/BI
          OR TETRACYCLIC?/BI) AND L29
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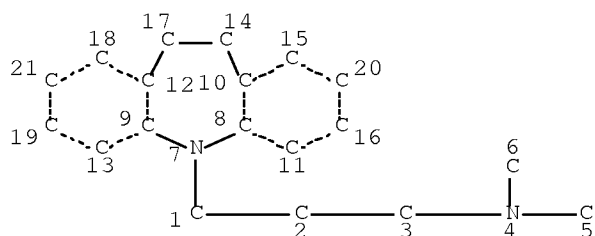
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          E OR TRIMIPRAMINE)/CN
L13        3 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (DESIPRAMINE OR
          NORTRIPTYLINE OR PROTRIPTYLINE)/CN
L14        6 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (DEMEXIPTILINE OR
          DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR
          METAPRAMINE)/CN
L15        4 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (NITROXAZEPINE OR
          NOXIPTILINE OR PROPIZEPINE OR QUINUPRAMINE)/CN
L16        6 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (AMINEPTINE OR
          OPIPRAMOL OR TIANEPTINE OR CIANOPRAMINE OR CYANODOTHIEPIN OR
          FLUOTRACEN)/CN
L17       25 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (L12 OR L13 OR L14
          OR L15 OR L16)
L19        6 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  (AMOXAPINE OR
          MAPROTILINE OR MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR
          OXAPROTILINE)/CN
L24      15309 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ?CYSTIC FIBROS?/BI
L25        609 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROCYSTIC?/BI OR
          FIBRO CYSTIC?/BI
L26        155 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  MUCOVISCIDOSIS/BI
L27        5892 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  CFTR/BI
L28      15430 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  FIBROSIS/BI (L)
          CYSTIC/BI
L29      16341 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR
          L27 OR L28)
L34       31 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L17 OR L19
L36       11 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L34 AND L29
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=> d stat que L37

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L4      STR
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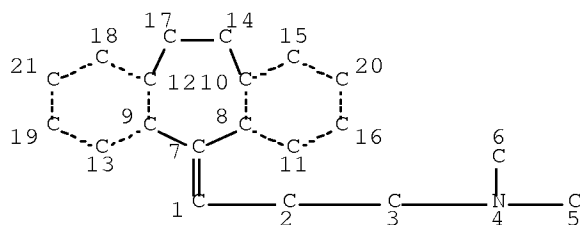
10/524815



NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE  
 L5 STR



NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L7	135	SEA FILE=REGISTRY FAM FUL L4				
L9	83	SEA FILE=REGISTRY FAM FUL L5				
L24	15309	SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON	?CYSTIC FIBROS?/BI			
L25	609	SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON	FIBROCYSTIC?/BI OR			
			FIBRO CYSTIC?/BI			
L26	155	SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON	MUCOVISCIDOSIS/BI			
L27	5892	SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON	CFTR/BI			
L28	15430	SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON	FIBROSIS/BI (L)			
			CYSTIC/BI			
L29	16341	SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON	(L24 OR L25 OR L26 OR			
			L27 OR L28)			
L37	12	SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON	(L7 OR L9) AND L29			

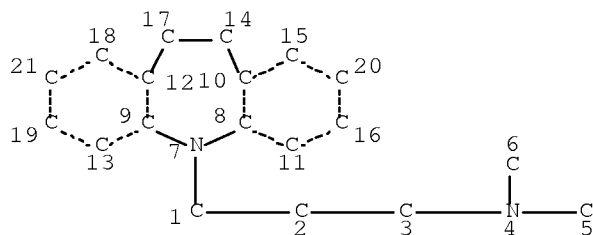
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 L90 22 L32 OR L36 OR L37

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=> file medline embase biosis
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=> d stat que L58
L4          STR
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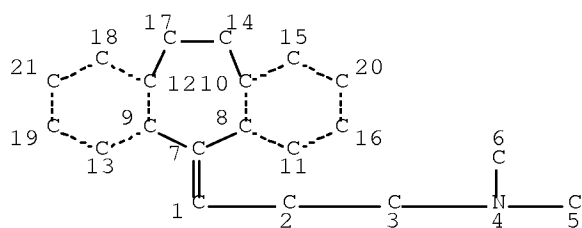
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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 21

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STEREO ATTRIBUTES: NONE
L5                      STR
```



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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L7	135	SEA FILE=REGISTRY FAM FUL	L4
L9	83	SEA FILE=REGISTRY FAM FUL	L5
L12	6	SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR CLOMIPRAMINE OR DOSULEPIN OR DOTHIEPIN OR DOXEPIN OR LOFEPRAMIN	

10/524815

E OR TRIMIPRAMINE)/CN  
L13 3 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DESIPRAMINE OR  
NORTRIPTYLINE OR PROTRIPTYLINE)/CN  
L14 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR  
DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR  
METAPRAMINE)/CN  
L15 4 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR  
NOXIPTILINE OR PROPIZEPINE OR QUINUPRAMINE)/CN  
L16 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMINEPTINE OR  
OPIPRAMOL OR TIANEPTINE OR CIANOPRAMINE OR CYANODOTHIEPIN OR  
FLUOTRACEN)/CN  
L17 25 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (L12 OR L13 OR L14  
OR L15 OR L16)  
L19 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMOXAPINE OR  
MAPROTILINE OR MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR  
OXAPROTILINE)/CN  
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L25 609 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROCYSTIC?/BI OR  
FIBRO CYSTIC?/BI  
L26 155 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON MUCOVISCIDOSIS/BI  
L27 5892 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON CFTR/BI  
L28 15430 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROSIS/BI (L)  
CYSTIC/BI  
L29 16341 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON (L24 OR L25 OR L26 OR  
L27 OR L28)  
L34 31 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON L17 OR L19  
L45 218 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON L7 OR L9  
L46 SEL PLU=ON L45 1- CHEM : 409 TERMS  
L47 78135 SEA L46  
L48 96337 SEA L29  
L49 39 SEA L47 AND L48  
L52 SEL PLU=ON L34 1- CHEM : 233 TERMS  
L53 91067 SEA L52  
L54 25 SEA L53 AND L29  
L56 24 SEA (TRICYCLIC OR TETRACYCLIC)/BI AND L29  
L57 75 SEA L49 OR L54 OR L56  
L58 31 SEA L57 AND PY<2004

=> dup rem L90 L58

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PROCESSING COMPLETED FOR L90  
PROCESSING COMPLETED FOR L58

L91 49 DUP REM L90 L58 (4 DUPLICATES REMOVED)  
ANSWERS '1-22' FROM FILE ZCAPLUS  
ANSWERS '23-27' FROM FILE MEDLINE  
ANSWERS '28-48' FROM FILE EMBASE  
ANSWER '49' FROM FILE BIOSIS

10/524815

=> d ibib abs hitind hitstr L91 1-22; d iall L91 23-49

L91 ANSWER 1 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2009:1044258 ZCAPLUS Full-text  
DOCUMENT NUMBER: 151:297806  
TITLE: Methods and compositions for the treatment of  
disorders associated with defects of the cystic  
fibrosis transmembrane conductance regulator gene or  
protein  
INVENTOR(S): Lin, Stephen; Staunton, Jane; Sui, Jinliang  
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA  
SOURCE: PCT Int. Appl., 108pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2009105234	A2	20090827	WO 2009-US1061	20090219
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2008-66259P P 20080219  
AB The present invention features compns., methods, and kits for treating, or ameliorating disorders associated with a defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or protein (e.g., cystic fibrosis).  
CC 63-5 (Pharmaceuticals)  
Section cross-reference(s): 6  
ST defect cystic fibrosis transmembrane conductance regulator gene protein CFTR  
IT Gene, animal  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CFTR; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)  
IT Essential oils  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Clary sage; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)  
IT Essential oils  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cedarwood; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)  
IT Essential oils  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (clove; methods and compns. for treatment of disorders associated with



- defects of **cystic fibrosis** transmembrane  
conductance regulator gene or protein)
- IT **Cystic fibrosis**  
Drug design  
Drug screening  
Drug targets  
HMG-CoA reductase inhibitors  
Human  
Inhalation drug delivery systems  
Leiurus quinquestriatus  
Oral drug delivery systems  
(methods and compns. for treatment of disorders associated with defects of  
**cystic fibrosis** transmembrane conductance regulator  
gene or protein)
- IT **CFTR** (**cystic fibrosis** transmembrane  
conductance regulator)  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(methods and compns. for treatment of disorders associated with defects of  
**cystic fibrosis** transmembrane conductance regulator  
gene or protein)
- IT **Flavonoids**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and compns. for treatment of disorders associated with defects of  
**cystic fibrosis** transmembrane conductance regulator  
gene or protein)
- IT **Steroids**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods and compns. for treatment of disorders associated with defects of  
**cystic fibrosis** transmembrane conductance regulator  
gene or protein)
- IT 853220-52-7  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(APWAG1; methods and compns. for treatment of disorders associated with  
defects of **cystic fibrosis** transmembrane  
conductance regulator gene or protein)
- IT 95907-66-7D, Quinoxalinecarboxylic acid, derivs.  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BML-257; methods and compns. for treatment of disorders associated with  
defects of **cystic fibrosis** transmembrane  
conductance regulator gene or protein)
- IT 2390-54-7D, derivs.  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BTA-1; methods and compns. for treatment of disorders associated with  
defects of **cystic fibrosis** transmembrane  
conductance regulator gene or protein)
- IT 77-10-1D, derivs., hydrochlorides  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BTCP; methods and compns. for treatment of disorders associated with  
defects of **cystic fibrosis** transmembrane  
conductance regulator gene or protein)
- IT 331-39-5D, Caffeic acid, derivative  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CAPE; methods and compns. for treatment of disorders associated with  
defects of **cystic fibrosis** transmembrane  
conductance regulator gene or protein)
- IT 119-65-3D, Isoquinoline, derivative  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CBIQ; methods and compns. for treatment of disorders associated with  
defects of **cystic fibrosis** transmembrane  
conductance regulator gene or protein)

- IT 51-17-2D, Benzimidazole, derivative  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (DCEBIO; methods and compns. for treatment of disorders associated with defects of **cystic fibrosis** transmembrane conductance regulator gene or protein)
- IT 289-95-2D, Pyrimidine, derivative  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (PP2; methods and compns. for treatment of disorders associated with defects of **cystic fibrosis** transmembrane conductance regulator gene or protein)
- IT 9076-57-7, Histone deacetylase 26833-87-4, Homoharringtonine  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitor III; methods and compns. for treatment of disorders associated with defects of **cystic fibrosis** transmembrane conductance regulator gene or protein)
- IT 155215-87-5  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitor; methods and compns. for treatment of disorders associated with defects of **cystic fibrosis** transmembrane conductance regulator gene or protein)
- IT 131384-38-8, Farnesyltransferase  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibitor; methods and compns. for treatment of disorders associated with defects of **cystic fibrosis** transmembrane conductance regulator gene or protein)
- IT 9028-35-7  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibitors; methods and compns. for treatment of disorders associated with defects of **cystic fibrosis** transmembrane conductance regulator gene or protein)
- IT 50-22-6, Corticosterone 50-27-1, Estriol 50-28-2, Estradiol, biological studies ~~50-48-6~~, Amitriptyline 50-76-0, Dactinomycin 53-19-0, Mitotane 53-34-9, Fluprednisolone 54-11-5, Nicotine 56-53-1, Diethylstilbestrol 57-63-6, Ethinyl estradiol 57-91-0, Alfatradiol 58-33-3, Promethazine hydrochloride 58-46-8, Tetrabenazine 58-89-9, Lindane 59-96-1 60-82-2, Phloretin 66-97-7, Psoralen 68-88-2, Hydroxyzine 70-30-4, Hexachlorophene 71-62-5, Veratridine ~~72-69-5~~, Nortriptyline 72-80-0, Chlorquinaldol 75-05-8, Acetonitrile, biological studies 79-78-7, Allyl  $\alpha$ -ionone 83-79-4, Rotenone 84-17-3, Dienestrol 89-68-9, Chlorothymol 92-84-2, Phenothiazine 94-18-8, Benzylparaben 94-41-7, Chalcone 94-78-0, Phenazopyridine 97-18-7, Bithionol 97-23-4, Dichlorophen 97-24-5, Fenticlor 99-66-1, Valproic acid 103-16-2, Monobenzene 111-87-5, 1-Octanol, biological studies 113-59-7, Chlorprothixene 117-39-5, Quercetin 120-32-1, Clorofene 123-03-5, Cetylpyridinium chloride 124-94-7, Triamcinolone 125-69-9, Dextromethorphan hydrobromide 127-31-1, Fludrocortisone 129-03-3 130-61-0, Thioridazine hydrochloride 131-53-3 136-47-0, Tetracaine hydrochloride 140-95-4 148-82-3, Melphalan 152-43-2, Quinestrol 298-57-7, Cinnarizine ~~303-49-1~~, Clomipramine 313-04-2, Desmosterol 356-12-7, Fluocinonide 362-07-2 378-44-9, Betamethasone 402-71-1, TPCK 434-22-0, Nandrolone 439-14-5, Diazepam 440-17-5, Trifluoperazine hydrochloride 446-72-0, Genistein 483-18-1, Emetine 520-36-5, Apigenin 524-95-8 528-48-3, Fisetin 541-19-5, Suxamethonium iodide 553-08-2, Thonzonium bromide 579-23-7 583-03-9, Fenipentol 638-94-8, Desonide 719-59-5 777-11-7, Haloprogin 863-61-6, Menatetrenone 961-29-5, Isoliquiritigenin 982-57-0, Chloramphenicol sodium succinate 985-13-7, Ethaverine hydrochloride 1034-01-1, Octyl gallate 1098-60-8, Triflupromazine hydrochloride 1404-04-2, Neomycin 1420-55-9 ~~1668-19-5~~, Doxepin 1716-12-7, Sodium Phenylbutyrate 1744-22-5,

Riluzole 1841-19-6, Fluspirilene 1951-25-3, Amiodarone 2062-78-4,  
 Pimozide 2210-63-1, Mofebutazone 2616-71-9, CHenodeoxycholic acid  
 diacetate Methyl ester 2668-66-8, Medrysone 2799-07-7,  
 S-Trityl-L-cysteine 3039-71-2, U18666A 3703-76-2, Cloperastine  
 3737-09-5, Disopyramide 3810-80-8, Diphenoxylate hydrochloride  
 4419-39-0, Beclomethasone 4431-00-9, Aurintricarboxylic acid  
 4547-24-4, Corosolic acid 5466-77-3, Octyl methoxycinnamate 5610-40-2,  
 Securinine 5653-80-5, (+/-)-Methadone 5812-07-7, SU4312 6164-47-2,  
 Protopine hydrochloride 6621-47-2, Perhexiline 7059-24-7, Chromomycin  
 A3 7770-78-7, (-)-Arctigenin 8044-71-1, Cetrime 9004-32-4,  
 Carboxymethyl-cellulose 10540-29-1, Tamoxifen 11103-72-3, Ruthenium  
 red 13042-18-7, Fendiline 13598-51-1D, Phosphorothioic acid,  
 bicyclo[2.2.2] derivative, tert-Bu ester 13739-02-1, Diacerein 14009-24-6,  
 Drotaverine 14484-47-0, Deflazacort 14779-78-3, Padimate 14937-32-7  
 15278-97-4, Chloro(trimethyl-phosphine) gold 15301-69-6, Flavoxate  
 15442-64-5, Zinc protoporphyrin 15686-51-8, Clemastine 16590-41-3,  
 Naltrexone 17348-76-4, 2'-Hydroxyflavanone 18378-89-7, Plicamycin  
 18417-89-5, Sangivamycin 18917-93-6, Magnesium lactate 19428-14-9  
 19774-82-4, Amiodarone hydrochloride 21829-25-4, Nifedipine 22345-47-7  
 22784-59-4, trans-Benzyl(chloro)-bis(triphenylphosphine) palladium  
 22916-47-8, Miconazole 23214-92-8, Doxorubicin 23593-75-1,  
 Clotrimazole 24356-60-3, Cephapirin sodium 26095-59-0, Otilonium  
 bromide 26787-78-0, Amoxicillin 26864-56-2, Penfluridol 27220-47-9,  
 Econazole 27790-75-6, Dihydropyridine 29767-20-2, Teniposide  
 30562-34-6, Geldanamycin 31282-04-9, Hygromycin B 31384-98-2,  
 N-Salicyloyltryptamine 31883-05-3, Moricizine 32981-86-5,  
 10-Deacetylbaicatin III 33016-12-5, TN-16 33342-05-1, Gliquidone  
 34031-32-8, Auranofin 34552-83-5, Loperamide hydrochloride 34823-86-4,  
 GTP-14564 36945-98-9, Icilin 37693-01-9, Clofoctol 37739-05-2,  
 2-Chloro-N6-cyclopentyl adenosine 38194-50-2 38239-56-4D, 4'-boranyl  
 derivative 39562-70-4, Nitrendipine 42399-41-7, (+)-cis-Diltiazem  
 42461-84-7, Flunixin meglumine 42924-53-8, Nabumetone 49562-28-9,  
 Fenofibrate 49697-38-3, Rimexolone 50847-11-5, Ibudilast 51022-77-6  
 51264-14-3, Amsacrine 51333-22-3, Budesonide 51781-06-7, Carteolol  
 52468-60-7, Flunarizine 52645-53-1 53016-31-2, Norelgestromin  
 53123-88-9, Sirolimus 53370-90-4, Exalamide 53938-07-1, Viburnine  
 54024-22-5 54197-31-8 54965-21-8, Albendazole 55985-32-5,  
 Nicardipine 56420-45-2, Epirubicin 57381-26-7, Irsogladine  
 57808-66-9, Domperidone 58749-22-7, Licochalcone-A 59937-28-9,  
 Malotilate 60142-96-3, Gabapentin 60282-87-3, Gestodene 61413-54-5,  
 Rolipram 62571-86-2, Captopril 62996-74-1, Staurosporine 63653-99-6,  
 FS 2 63675-72-9, Nisoldipine 64706-54-3, Bepridil 64872-76-0,  
 Butoconazole 65472-88-0, Naftifine 65899-73-2 66085-59-4, Nimodipine  
 66575-29-9, Forskolin 66934-18-7 68506-86-5 68786-66-3,  
 Triclabendazole 70238-51-6 70288-86-7, Ivermectin 71145-03-4,  
 BAYK8644 71897-07-9, Tyrphostin Ag 1295 72509-76-3, Felodipine  
 74863-84-6, Argatroban 75330-75-5, Lovastatin 75593-17-8,  
 Debromo-hymenialdisine 75607-67-9, Fludarabine phosphate 75695-93-1,  
 Isradipine 75747-14-7, 17-AAG 78491-02-8, Diazolidinyl urea  
 79794-75-5, Loratadine 79855-88-2, Trequinsin 79902-63-9, Simvastatin  
 81117-35-3, N-Nonyldeoxynojirimycin 81166-47-4, DIOA 81226-60-0  
 82749-70-0, DCPIB 90357-06-5, Bicalutamide 91599-74-5, Benidipine  
 hydrochloride 93957-54-1, Fluvastatin 95734-82-0, Nedaplatin  
 98629-43-7, Gusperimus 100427-26-7, Lercanidipine 101477-55-8,  
 Lomerizine 101975-10-4, Zardaverine 102146-07-6,  
 8-Cyclopentyl-1,3-dipropylxanthine 102396-24-7, Jasplakinolide  
 103060-53-3, Daptomycin 103177-37-3, Pranlukast 103577-45-3,  
 Lansoprazole 103745-39-7, HA 1077 104615-18-1, CGS15943 104632-26-0,  
 Pramipexole 104757-53-1, Barnidipine hydrochloride 106266-06-2,  
 Risperidone 106328-57-8, BW-A4C 107254-86-4,

10/524815

5-Nitro-2-(3-phenyl-propylamino) benzoic acid

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treatment of disorders associated with defects of  
cystic fibrosis transmembrane conductance regulator  
gene or protein)

IT 107753-78-6, Zafirlukast 110429-36-2, N-Methyl-paroxetine 110588-57-3,  
Saperconazole 111470-99-6, Amlodipine besylate 112809-51-5, Letrozole  
112830-95-2, HU 210 113665-84-2, Clopidogrel 116666-63-8, Mibefradil  
dihydrochloride 117976-89-3, Rabeprazole 118457-14-0, Nebivolol  
120014-06-4, Donepezil 120934-96-5, FPL64176 121911-71-5 122320-73-4  
123318-82-1, Clofarabine 123524-52-7, Azelnidipine 123653-11-2, NS 398  
124753-97-5, C6-Ceramide 126544-47-6, Ciclesonide 130493-03-7,  
Bimoclomol 130495-35-1, SKF-96365 131543-22-1, WIN 55212-2  
132203-70-4, Cilnidipine 132861-87-1, PD81723 133343-34-7, Lactacystin  
133407-82-6, MG 132 133550-35-3, AG 494 134381-21-8, Epoxomicin  
134523-00-5, Atorvastatin 138605-00-2, NKH477 138989-57-8, RG 14620  
139755-83-2, Sildenafil 141797-92-4 145599-86-6, Cerivastatin  
145915-58-8 145915-60-2 147098-20-2, Rosuvastatin calcium  
148016-81-3, Doripenem 148741-30-4, AG 879 149647-78-9,  
Suberoylanilide hydroxamic acid 154447-36-6, LY294002 154598-52-4,  
Efavirenz 159351-69-6, Everolimus 160098-96-4, SCH58261 161814-49-9,  
Amprenavir 162401-32-3, Roflumilast 163222-33-1, Ezetimibe  
163515-35-3, Chlorotoxin 167869-21-8, PD98059 168835-82-3, SU1498  
169590-42-5, Celecoxib 179324-69-7, Bortezomib 180977-44-0, GGTI-298  
183506-66-3 186131-38-4, WP631 189197-69-1, Ro 48-8071 191102-87-1,  
GGTI-2147 191114-48-4, Telithromycin 192441-08-0, Lomeguatrib  
193551-00-7, CAY10398 193620-69-8, TAS-301 203460-30-4, SNX-482  
209783-80-2 212141-54-3, Vatalanib 212844-53-6, Purvalanol A  
218924-25-5, KNK-437 221877-54-9, Zotarolimus 223499-30-7, YM 58483  
224785-90-4 225235-77-8 239066-73-0, AL 438 269390-69-4  
287383-59-9, Scriptaid 287714-41-4, Rosuvastatin 289893-25-0,  
Arimoclomol 293754-55-9, TO 901317 298193-32-5 302962-49-8,  
Dasatinib 324526-70-7 357400-13-6, NNC55-0396 362000-44-0  
371935-74-9, PI-103 421580-53-2 433695-36-4, BRL-50481 439083-90-6,  
BAY60-7550 467214-20-6 496864-16-5, Aloisine A 537034-15-4  
544478-19-5, MRS1845 546141-08-6, URB597 623531-00-0 698387-09-6,  
Neratinib 749886-87-1 815592-21-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treatment of disorders associated with defects of  
cystic fibrosis transmembrane conductance regulator  
gene or protein)

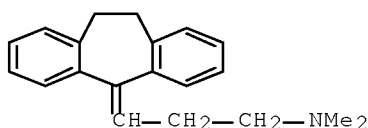
IT 50-48-6, Amitriptyline 72-69-5, Nortriptyline  
303-49-1, Clomipramine 1668-19-5, Doxepin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treatment of disorders associated with defects of  
cystic fibrosis transmembrane conductance regulator  
gene or protein)

RN 50-48-6 ZCAPLUS

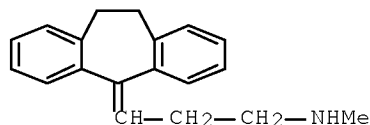
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-  
dimethyl- (CA INDEX NAME)



10/524815

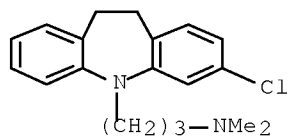
RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



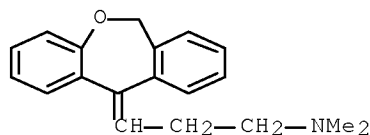
RN 303-49-1 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



L91 ANSWER 2 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:827242 ZCAPLUS Full-text

DOCUMENT NUMBER: 151:108500

TITLE: Pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants

INVENTOR(S): Gulbins, Erich

PATENT ASSIGNEE(S): Cynad GmbH & Co. KG, Germany

SOURCE: PCT Int. Appl., 54pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009083211	A2	20090709	WO 2008-EP10996	20081222
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
PRIORITY APPLN. INFO.:			DE 2007-102007063535A	20071221
AB	The invention relates to a pharmaceutical compound for the prophylaxis and/or symptomatic treatment of <b>cystic fibrosis</b> , particularly for the prophylaxis and/or treatment of infections and/or infection illnesses manifesting with <b>cystic fibrosis</b> , having at least one anti-depressive and preferable at least one dispersion agent and/or at least one pharmaceutically tolerated carrier material. Liquid dispersion media are used to prepare parenteral, especially inhalant delivery systems. Thus <b>Cftr</b> -knockout mice and wild-type mice were treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration			
IC	ICM A61K			
CC	63-6 (Pharmaceuticals)			
	Section cross-reference(s): 1, 14			
ST	<b>cystic fibrosis</b> antidepressant inhalant			
IT	5-HT reuptake inhibitors			
	Antidepressants			
	Burkholderia cepacia			
	<b>Cystic fibrosis</b>			
	Dopamine reuptake inhibitors			
	Haemophilus influenzae			
	Inhalation drug delivery systems			
	Lung			
	Noradrenaline reuptake inhibitors			
	Parenteral drug delivery systems			
	Pharmaceutical solutions			
	Prophylaxis			
	Pseudomonas aeruginosa			
	Staphylococcus aureus			
	Therapy			
	(pharmaceutical composition for prophylaxis and/or symptomatic treatment of <b>cystic fibrosis</b> with antidepressants)			
IT	Antibodies and Immunoglobulins			
	RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(pharmaceutical composition for prophylaxis and/or symptomatic treatment of <b>cystic fibrosis</b> with antidepressants)			
IT	111-57-9, Ceramid 9031-54-3, Sphingomyelinase			
	RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)			
	(pharmaceutical composition for prophylaxis and/or symptomatic treatment of <b>cystic fibrosis</b> with antidepressants)			
IT	50-67-9, Serotonin, biological studies 51-41-2, Noradrenalin 51-61-6, Dopamine, biological studies			
	RL: BSU (Biological study, unclassified); BIOL (Biological study)			

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of  
cystic fibrosis with antidepressants)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline  
50-49-7, Imipramine 58-40-2, Promazine 72-69-5,  
Nortriptyline 86-13-5, Benztropine 113-45-1, Methylphenidate  
129-03-3, Cyproheptadine 155-09-9, Tranylcypromine 256-96-2D,  
5H-Dibenz[b,f]azepine, derivative 303-49-1 303-53-7,  
Cyclobenzaprine 315-72-0 494-19-9,  
10,11-Dihydro-5H-dibenzo[b,f]azepine 739-71-9, Trimipramine  
911-45-5, Clomiphen 1668-19-5, Doxepine 4317-14-0,  
Amitriptyline oxide 4498-32-2, Dibenzepine 6621-47-2,  
Perhexiline 10262-69-8, Maprotiline 19794-93-5, Trazodon  
23047-25-8, Lofepramine 24219-97-4, Mianserin  
24526-64-5, Nomifensin 32359-34-5, Medifoxamine 34911-55-2, Bupropion  
46817-91-8, Viloxazine 54739-18-3, Fluvoxamine 57574-09-1,  
Amineptine 59729-33-8, Citalopram 61869-08-7, Paroxetine 71320-77-9,  
Moclobemide 71620-89-8, Reboxetine 72797-41-2, Tianeptine  
83366-66-9, Nefazodone 85650-52-8, Mirtazapine 92623-85-3,  
Milnacipran 93413-69-5, Venlafaxin 116539-59-4, Duloxetine  
128196-01-0, Escitalopram

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

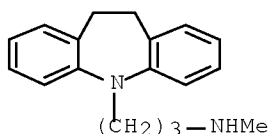
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of  
cystic fibrosis with antidepressants)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline  
50-49-7, Imipramine 72-69-5, Nortriptyline  
303-49-1 315-72-0 739-71-9, Trimipramine  
1668-19-5, Doxepine 4498-32-2, Dibenzepine  
10262-69-8, Maprotiline 23047-25-8, Lofepramine  
24219-97-4, Mianserin 57574-09-1, Amineptine  
72797-41-2, Tianeptine 85650-52-8, Mirtazapine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

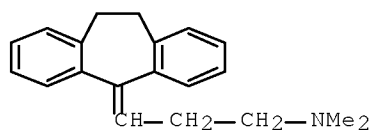
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of  
cystic fibrosis with antidepressants)

RN 50-47-5 ZCAPLUS  
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (CA INDEX  
NAME)

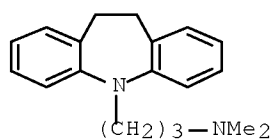


RN 50-48-6 ZCAPLUS  
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-  
dimethyl- (CA INDEX NAME)

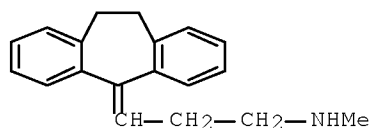
10/524815



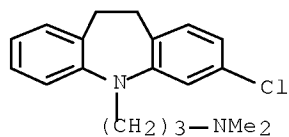
RN 50-49-7 ZCAPLUS  
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS  
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



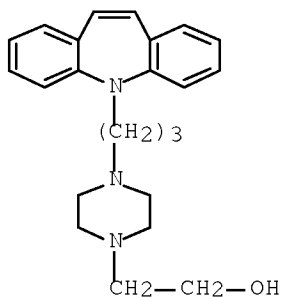
RN 303-49-1 ZCAPLUS  
CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 315-72-0 ZCAPLUS  
CN 1-Piperazineethanol, 4-[3-(5H-dibenz[b,f]azepin-5-yl)propyl]- (CA INDEX NAME)

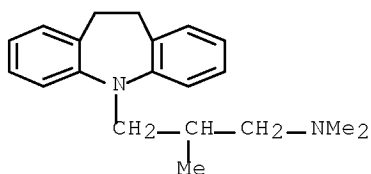


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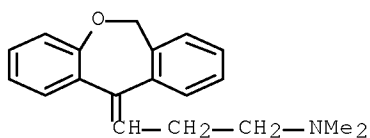
RN 739-71-9 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N,β-trimethyl-  
(CA INDEX NAME)



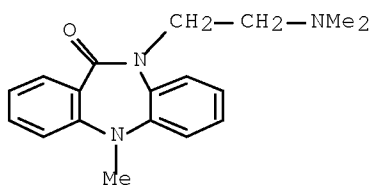
RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX  
NAME)



RN 4498-32-2 ZCAPLUS

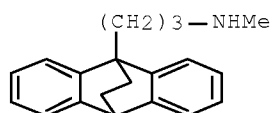
CN 11H-Dibenzo[b,e][1,4]diazepin-11-one,  
10-[2-(dimethylamino)ethyl]-5,10-dihydro-5-methyl- (CA INDEX NAME)



10/524815

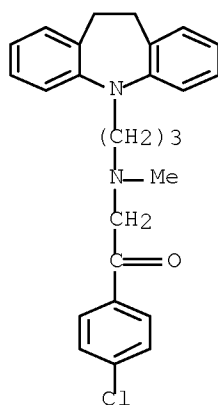
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CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



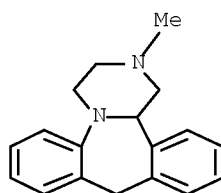
RN 23047-25-8 ZCAPLUS

CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]methylamino]- (CA INDEX NAME)



RN 24219-97-4 ZCAPLUS

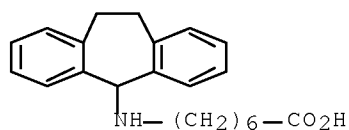
CN Dibenzo[c,f]pyrazino[1,2-a]azepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



RN 57574-09-1 ZCAPLUS

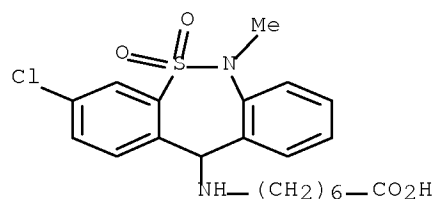
CN Heptanoic acid, 7-[(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)amino]- (CA INDEX NAME)

10/524815



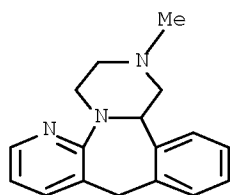
RN 72797-41-2 ZCAPLUS

CN Heptanoic acid, 7-[(3-chloro-6,11-dihydro-6-methyl-5,5-dioxidodibenzo[c,f][1,2]thiazepin-11-yl)amino]- (CA INDEX NAME)



RN 85650-52-8 ZCAPLUS

CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



L91 ANSWER 3 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:206116 ZCAPLUS Full-text

DOCUMENT NUMBER: 150:252701

TITLE: Therapeutic combinations useful in treating cystic fibrosis and other CFTR-related diseases

INVENTOR(S): Singh, Ashvani; Worley, Jennings Franklin., III; Zlokarnik, Gregor

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 65pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2009023509                      A2                      20090219                      WO 2008-US72446                      20080807

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

## PRIORITY APPLN. INFO.:

US 2007-954850P

P 20070809

AB The invention discloses therapeutic combinations and kits useful in treating CFTR-related diseases, such as cystic fibrosis. Combinations of the invention include e.g. ivermectin and N-(5-hydroxy-2,4-ditert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide.

CC 1-12 (Pharmacology)

ST CFTR disease cystic fibrosis combination treatment; quinoline carboxamide deriv combination ivermectin CFTR disease treatment

IT CFTR (cystic fibrosis transmembrane conductance regulator)

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(508-dephenylalanine-; therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT Mutation

(mutant CFTR; therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT CFTR (cystic fibrosis transmembrane conductance regulator)

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(mutant; therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT Antifibrotic agents

Combination chemotherapy

Cystic fibrosis

Drug delivery systems

Human

(therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT 16887-00-6, Chloride, biological studies

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT 50-41-9, Clomiphene citrate    50-52-2, Thioridazine    55-03-8, Levothyroxine sodium    58-33-3, Promethazine hydrochloride    58-39-9, Perphenazine    69-09-0, Chlorpromazine hydrochloride    83-43-2, Methylprednisolone    84-02-6, Prochlorperazine maleate    129-20-4, Oxyphenbutazone    154-42-7, Thioguanine    894-71-3, Nortriptyline hydrochloride    969-33-5, Cyproheptadine hydrochloride    1225-55-4, Protriptyline hydrochloride    1951-25-3, Amiodarone    3810-80-8, Diphenoxylate hydrochloride    4330-99-8, Trimeprazine tartrate    14028-44-5, Amoxapine    14976-57-9, Clemastine fumarate    17321-77-6, Chlorimipramine hydrochloride    19216-56-9    42971-09-5,

Vinpocetine 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54527-84-3, Nicardipine hydrochloride 55981-09-4, Nitazoxanide 59865-13-3, Cyclosporine A 64706-54-3, Bepridil 70288-86-7, Ivermectin 72956-09-3, Carvedilol 79794-75-5, Loratadine 84625-61-6, Itraconazole ~~85650-52-8~~, Mirtazapine 93957-55-2, Fluvastatin sodium 100643-71-8, Desloratadine 110429-35-1, Paroxetine hydrochloride hemihydrate 111470-99-6, Amlodipine besylate 116666-63-8, Mibefradil dihydrochloride 127779-20-8, Saquinavir 159989-65-8, Nelfinavir mesylate 163222-33-1, Ezetimibe 184475-35-2, Gefitinib 325779-54-2 329691-97-6 329691-99-8 329692-01-5 329692-03-7 329692-05-9 329692-14-0 775304-57-9 873050-18-1 873050-19-2 873050-20-5 873050-21-6 873050-22-7 873050-23-8 873050-24-9 873050-25-0 873050-26-1 873050-27-2 873050-28-3 873050-29-4 873050-30-7 873050-31-8 873050-32-9 873050-33-0 873050-34-1 873050-35-2 873050-36-3 873050-37-4 873050-38-5 873050-39-6 873050-40-9 873050-41-0 873050-42-1 873050-43-2 873050-44-3 873050-45-4 873050-46-5 873050-47-6 873050-48-7 873050-49-8 873050-50-1 873050-51-2 873050-52-3 873050-53-4 873050-54-5 873050-55-6 873050-56-7 873050-57-8 873050-58-9 873050-59-0 873050-60-3 873050-61-4 873050-62-5 873050-63-6 873050-64-7 873050-65-8 873050-66-9 873050-67-0 873050-68-1 873050-69-2 873050-70-5 873050-71-6 873050-72-7 873050-73-8 873050-74-9 873050-75-0 873050-76-1 873050-77-2 873050-78-3 873050-79-4 873050-80-7 873050-81-8 873050-82-9 873050-83-0 873050-84-1 873050-85-2 873050-86-3 873050-87-4 873050-88-5 873050-89-6 873050-90-9 873050-91-0 873050-92-1 873050-93-2 873050-94-3 873050-95-4 873050-96-5 873050-97-6 873050-98-7 873050-99-8 873051-00-4 873051-01-5 873051-02-6 873051-03-7 873051-04-8 873051-05-9 873051-06-0 873051-07-1 873051-08-2 873051-09-3 873051-10-6 873051-11-7 873051-12-8 873051-13-9 873051-14-0 873051-15-1 873051-16-2 873051-17-3 873051-18-4 873051-19-5 873051-20-8 873051-21-9 873051-22-0 873051-23-1 873051-24-2 873051-25-3 873051-26-4 873051-27-5 873051-28-6 873051-29-7 873051-30-0 873051-31-1 873051-32-2 873051-33-3 873051-34-4 873051-35-5 873051-36-6 873051-37-7 873051-38-8 873051-39-9 873051-40-2 873051-41-3 873051-42-4 873051-43-5 873051-44-6 873051-45-7 873051-46-8 873051-47-9 873051-48-0 873051-49-1 873051-50-4 873051-51-5 873051-52-6 873051-54-8 873051-55-9 873051-56-0 873051-57-1 873051-58-2 873051-59-3 873051-60-6 873051-61-7 873051-62-8 873051-63-9 873051-64-0 873051-65-1 873051-66-2 873051-67-3 873051-68-4 873051-69-5 873051-70-8 873051-71-9 873051-72-0 873051-73-1 873051-75-3 873051-76-4 873051-77-5 873051-78-6 873051-79-7 873051-80-0 873051-81-1 873051-82-2 873051-83-3 873051-84-4 873051-85-5 873051-86-6 873051-87-7 873051-88-8 873051-89-9 873051-90-2 873051-91-3 873051-92-4 873051-93-5 873051-94-6 873051-95-7 873051-96-8 873051-97-9 873051-98-0 873051-99-1 873052-00-7 873052-01-8 873052-02-9 873052-03-0 873052-04-1 873052-05-2 873052-06-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(therapeutic combinations for treatment of **cystic  
fibrosis** and other **CFTR**-related diseases)

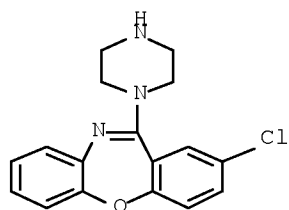
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

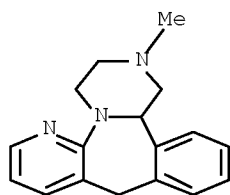
(therapeutic combinations for treatment of **cystic  
fibrosis** and other **CFTR**-related diseases)

10/524815

IT 14028-44-5, Amoxapine 85650-52-8, Mirtazapine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(therapeutic combinations for treatment of cystic  
fibrosis and other CFTR-related diseases)  
RN 14028-44-5 ZCAPLUS  
CN Dibenz[b,f][1,4]oxazepine, 2-chloro-11-(1-piperazinyl)- (CA INDEX NAME)



RN 85650-52-8 ZCAPLUS  
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine,  
1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



L91 ANSWER 4 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2009:549944 ZCAPLUS Full-text  
DOCUMENT NUMBER: 150:489908  
TITLE: System, method, and apparatus for storing, retrieving,  
and integrating clinical, diagnostic, genomic, and  
therapeutic data  
INVENTOR(S): Davies, Richard J.; Batye, Rick  
PATENT ASSIGNEE(S): MD Datacor, Inc., USA  
SOURCE: U.S., 55pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
US 7529685	B2	20090505	US 2001-983289	20011023
PRIORITY APPLN. INFO.:			US 2001-315020P	P 20010828
AB	A method, system, and computer program product for storing and retrieving patient data in a database connected to a network is disclosed. The method comprises storing clin. data in the database, extracting data from the clin.			

data, querying the database using a taxonomy that includes inclusive or exclusive search criterion, and receiving a result set. The method comprises creating a taxonomy that includes at least one search criterion; sending a query to the database, the query including said at least one search criteria; receiving the result set in response to the query, the result set including at least one result record; and displaying said at least one result record. The method, system, and computer program product can further include a user such as a clin. researcher, a treating physician, or a consulting physician analyzing the result set. A physician enters clin. information into the system about a patient being treated with azathioprine for arthritis developing anemia and showing neg. for GI bleeding. The system generates a result set that includes a suggestion to the physician to test the patient for a mutation in her thiopurine S-methyltransferase (TPMT) gene locus. The patient is found to be heterozygous for mutant TPMT which results in severe hematopoietic toxicity and resultant anemia. The system suggests alternative non-TPMT metabolized antiarthritic medication.

INCL 705003000; 707005000; 704009000

CC 9-1 (Biochemical Methods)

Section cross-reference(s): 1, 3, 14

IT Cystic fibrosis

(and modifier genes; system, method, and apparatus for storing, retrieving, and integrating clin., diagnostic, genomic, and therapeutic data)

IT 549-18-8, Elavil 56296-78-7, Prozac

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(depression treatment with, CYP2D6 variant in relation to; system, method, and apparatus for storing, retrieving, and integrating clin., diagnostic, genomic, and therapeutic data)

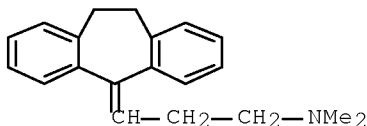
IT 549-18-8, Elavil

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(depression treatment with, CYP2D6 variant in relation to; system, method, and apparatus for storing, retrieving, and integrating clin., diagnostic, genomic, and therapeutic data)

RN 549-18-8 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 5 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:765170 ZCAPLUS Full-text

DOCUMENT NUMBER: 151:42088

TITLE: Pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants



10/524815

PATENT ASSIGNEE(S): Cycnad G.m.b.H. & Co. K.-G., Germany  
 SOURCE: Ger. Offen., 12pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
WO 2009083211	A2	20090709	WO 2008-EP10996	20081222

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DE 2007-102007063535A 20071221

AB The invention concerns a pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis, in particular for prophylaxis and/or treatment of cystic fibrosis related infections and/or infectious diseases, comprising at least one antidepressant and at least one dispersion medium. Liquid dispersion media are used to prepare parenteral, especially inhalant delivery systems. Thus Cftr-knockout mice and wild-type mice were treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 14

ST cystic fibrosis antidepressant inhalant

IT Antidepressants

Burkholderia cepacia

Cystic fibrosis

Haemophilus influenzae

Inhalation drug delivery systems

Lung

Parenteral drug delivery systems

Pharmaceutical solutions

Prophylaxis

Pseudomonas aeruginosa

Staphylococcus aureus

Therapy

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT Antibodies and Immunoglobulins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT 480-49-9, Filipin 1400-61-9, Nystatin 7585-39-9,  $\beta$ -Cyclodextrin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(in combination with; pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with

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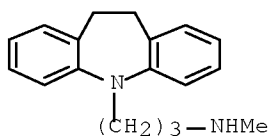
antidepressants)

IT 111-57-9, Ceramid 9031-54-3, Sphingomyelinase  
 RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)  
 (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

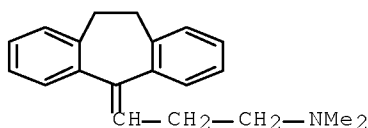
IT 50-47-5, Desipramine 50-48-6, Amitriptyline  
 50-49-7, Imipramine 72-69-5, Nortriptyline  
 256-96-2D, 5H-Dibenz[b,f]azepine, derivative 303-49-1  
 315-72-0 494-19-9, 10,11-Dihydro-5H-dibenzo[b,f]azepine  
 739-71-9, Trimipramine 1668-19-5, Doxepine  
 4317-14-0, Amitriptyline oxide 4498-32-2, Dibenzepine  
 10262-69-8, Maprotiline 23047-25-8, Lofepramine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline  
 50-49-7, Imipramine 72-69-5, Nortriptyline  
 303-49-1 315-72-0 739-71-9, Trimipramine  
 1668-19-5, Doxepine 4498-32-2, Dibenzepine  
 10262-69-8, Maprotiline 23047-25-8, Lofepramine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

RN 50-47-5 ZCAPLUS  
 CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (CA INDEX NAME)

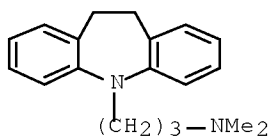


RN 50-48-6 ZCAPLUS  
 CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



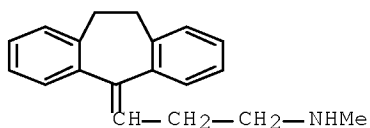
RN 50-49-7 ZCAPLUS  
 CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)

10/524815



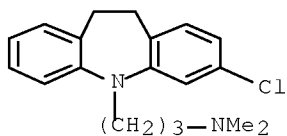
RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



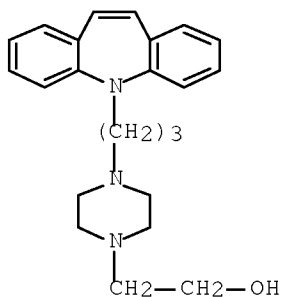
RN 303-49-1 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 315-72-0 ZCAPLUS

CN 1-Piperazineethanol, 4-[3-(5H-dibenz[b,f]azepin-5-yl)propyl]- (CA INDEX NAME)

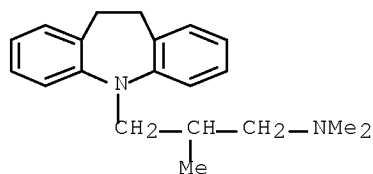


RN 739-71-9 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N,β-trimethyl-

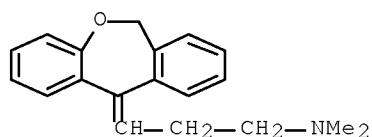
10/524815

(CA INDEX NAME)



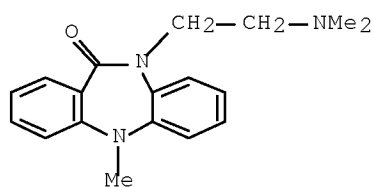
RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



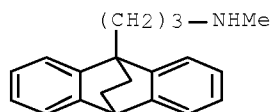
RN 4498-32-2 ZCAPLUS

CN 11H-Dibenzo[b,e][1,4]diazepin-11-one, 10-[2-(dimethylamino)ethyl]-5,10-dihydro-5-methyl- (CA INDEX NAME)



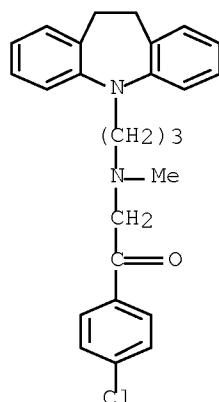
RN 10262-69-8 ZCAPLUS

CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



RN 23047-25-8 ZCAPLUS

CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]methylamino]- (CA INDEX NAME)

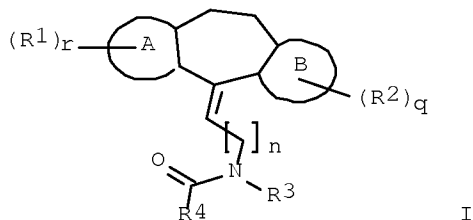


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 6 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2008:1211489 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 149:440406  
 TITLE: Methods of using tricyclic compounds in treating sodium channel-mediated diseases or conditions  
 INVENTOR(S): Kamboj, Rajender; Fraser, Robert; Fu, Jianmin; Kodumuru, Vishnumurthy; Sadalapure, Kashinath  
 PATENT ASSIGNEE(S): Xenon Pharmaceuticals Inc., Can.  
 SOURCE: PCT Int. Appl., 111pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008121859	A1	20081009	WO 2008-US58728	20080328
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2007-909091P P 20070330  
 OTHER SOURCE(S): CASREACT 149:440406; MARPAT 149:440406  
 GI



- AB This invention discloses tricyclic compds. I [ $n = 1-3$ ;  $r, q = 0-4$ ; A, B = fused (hetero)aryl;  $R_1, R_2$  = alkyl, alkenyl, halo, etc.;  $R_3$  = H, alkyl, alkenyl, etc.;  $R_4$  = H, alkyl, halo, etc.], as a stereoisomer, enantiomer, tautomer thereof or mixts. thereof, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as well as pharmaceutical compns. comprising the compds. and methods for using the compds. and the pharmaceutical compns. for the treatment and/or prevention of sodium channel-mediated diseases or conditions, e.g. pain cardiovascular diseases, respiratory diseases, etc. Preparation of e.g. 3-chloro-N-[3-(10,11-dihydro-5H-dibenzo[a,d][7]annulen-5-ylidene)propyl]-N-methylthiophene-2-carboxamide is described.
- CC 1-12 (Pharmacology)  
Section cross-reference(s): 27, 63
- ST tricyclic compd sodium channel disease treatment; sodium channel pain treatment tricyclic compd; cardiovascular respiratory disease treatment tricyclic compd; dibenzoannulenylidene deriv prepn sodium channel disease treatment
- IT Anti-AIDS agents  
Antiviral agents  
Drug toxicity  
(HIV treatment-induced neuropathy; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(Nav1.7; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(Nav1.8; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(Nav1.9; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(Nav1.2; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(Nav1.4; tricyclic compds. for treatment of sodium channel-mediated diseases)

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- IT Voltage-gated sodium channels  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(Nav1.5; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Antiarteriosclerotics  
(antiatherosclerotics; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Prostate gland disease  
(benign hyperplasia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Neoplasm  
(cancer pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Central nervous system  
(centrally mediated pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Headache  
(chronic, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain  
(chronic; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease  
(diabetic neuropathy; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Viscera  
(disease, pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nervous system, disease  
(dystonia, paroxysmal; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal  
(eudynia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal  
(familial erythralgia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Rectum  
(familial rectal pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Muscle, disease  
(fibromyalgia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Temperature effects, biological  
(heat, heat sensitivity; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain  
(inflammatory pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Fever and Hyperthermia  
(malignant; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Headache  
(migraine, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal  
(myasthenia syndromes; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Muscle, disease

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- (myotonia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nervous system, disease
  - (neural trauma; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
  - Pain
    - (neuralgia, post-herpetic; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Bladder disease
  - (neurogenic bladder pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
  - (neuropathic pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
  - (neuropathy, HIV treatment-induced neuropathy; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
  - (neuropathy, peripheral; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Surgery
  - (pain associated with or after; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Chemotherapy
  - Human immunodeficiency virus
  - Multiple sclerosis
  - Parturition
  - Ulcerative colitis
    - (pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Seizures
  - (partial and general tonic seizures; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
  - (peripheral nerve injury; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Injury
  - (peripheral nerve; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Peripheral nervous system
  - (peripherally mediated pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
  - (persistent; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
  - (phantom limb; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal
  - (primary eythermalgia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Aldosteronism
  - (pseudoaldosteronism; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Leg, disease
  - Sleep disorders
    - (restless leg syndrome; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Muscle, disease



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(rhabdomyolysis; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Headache  
(sinus, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Toxins  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(sodium channel toxin-related illnesses; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Sodium channels  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(sodium channel toxin-related illnesses; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Headache  
(tension, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Injury  
(trauma, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Amyotrophic lateral sclerosis

Analgesics

Anti-ischemic agents

Antiarrhythmics

Antiarthritics

Anticholesteremic agents

Anticonvulsants

Antidepressants

Antifibrotic agents

Antipsychotics

Antirheumatic agents

Antitumor agents

Anxiety

Anxiolytics

Arthritis

Atherosclerosis

Atrial fibrillation

Bipolar disorder

Cardiac arrhythmia

Cardiovascular agents

Cardiovascular disease

Crohn disease

Cystic fibrosis

Cytotoxic agents

Depression

Dermatological agents

Epilepsy

Gastrointestinal agents

Human

Hypercholesterolemia

Hypothyroidism

Irritable bowel syndrome

Ischemia

Mental and behavioral disorders

Neoplasm

Nervous system agents

Neuroprotective agents

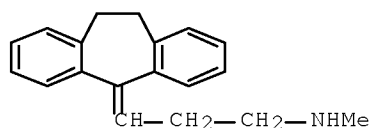
Osteoarthritis

Pain

Prodrugs

10/524815

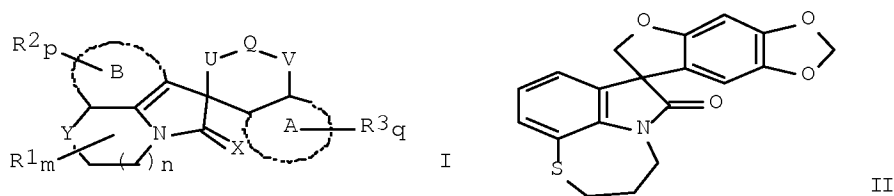
Prophylaxis  
Pruritus  
Psychotropics  
Respiratory system agents  
Respiratory system disease  
Rheumatoid arthritis  
Sarcoidosis  
Schizophrenia  
Sodium channel blockers  
Stroke  
Tachycardia  
Ventricular fibrillation  
    (tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT Voltage-gated sodium channels  
    RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
    (tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT Nerve, disease  
    Pain  
        (trigeminal neuralgia; tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT Disease, animal  
    (visceral pain; tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT Pain  
    (visceral; tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT 57-88-5, Cholesterol, biological studies  
    RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
    (tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT 1067431-34-8P   1067431-37-1P   1067431-40-6P   1067431-43-9P  
    1067431-46-2P   1067431-49-5P   1067431-52-0P   1067431-55-3P  
    1067431-58-6P   1067431-61-1P   1067431-64-4P  
    RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
    (tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT ~~72-69-5~~   59337-89-2  
    RL: RCT (Reactant); RACT (Reactant or reagent)  
    (tricyclic compds. for treatment of sodium channel-mediated diseases)  
IT ~~72-69-5~~  
    RL: RCT (Reactant); RACT (Reactant or reagent)  
    (tricyclic compds. for treatment of sodium channel-mediated diseases)  
RN 72-69-5   ZCAPLUS  
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 7 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2008:473340 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 148:472085  
 TITLE: Preparation of tricyclic spiro-oxindole derivatives  
 use as therapeutic agents  
 INVENTOR(S): Chafeev, Mikhail; Chowdhury, Sultan; Fu, Jianmin;  
 Kamboj, Rajender  
 PATENT ASSIGNEE(S): Xenon Pharmaceuticals Inc., Can.  
 SOURCE: PCT Int. Appl., 138 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008046046	A1	20080417	WO 2007-US81240	20071012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007307635	A1	20080417	AU 2007-307635	20071012
CA 2666136	A1	20080417	CA 2007-2666136	20071012
EP 2076518	A1	20090708	EP 2007-844222	20071012
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR				
MX 2009003874	A	20090422	MX 2009-3874	20090408
CN 101522685	A	20090902	CN 2007-80037642	20090408
IN 2009DN02456	A	20090619	IN 2009-DN2456	20090415
PRIORITY APPLN. INFO.:			US 2006-851190P	P 20061012
			WO 2007-US81240	W 20071012
OTHER SOURCE(S):			MARPAT 148:472085	
GI				



- AB Title compds. represented by the formula I [wherein U = (CH<sub>2</sub>)<sub>k</sub>; V = (CH<sub>2</sub>)<sub>j</sub>; j, k, p = independently 0-3; q = 1-4; m = 0-2; n = 0-4; Q = O, amino, SO, etc.; X = O or S; ring A = fused (hetero)aryl or fused heterocyclyl; ring B = fused (hetero)aryl or fused heterocyclyl; Y = CO, O, CF<sub>2</sub>, etc.; R<sub>1</sub> = independently halo, alkyl, aryl, etc.; R<sub>2</sub> = independently H, halo, alkyl, etc.; R<sub>3</sub> = independently H, (halo)alkyl, alkynyl, etc.; and stereoisomers, enantiomers, tautomers thereof or mixts. thereof; or pharmaceutically acceptable salts, solvates or prodrugs thereof] were prepared as sodium-channel blockers. For example, II was provided in a multi-step synthesis starting from 2,3,4,5-tetrahydrobenzo[b][1,4]thiazepine. I were tested in guanidine influx assay, and other biol. assay methods were described as well. Thus, I and their pharmaceutical compns. are useful for the treatment and/or prevention of sodium channel-mediated diseases or conditions, such as pain.
- CC 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63
- ST **tricyclic spiro oxindole** prepn sodium channel blocker pain treatment
- IT Pain  
(HIV; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Pain  
(acute, eudynia; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Antiarteriosclerotics  
(antiatherosclerotics; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Pain  
(associated with multiple sclerosis; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Prostate gland disease  
(benign hyperplasia; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Pain  
(cancer; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Pain  
(centrally mediated; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Pain  
(chemotherapy; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Pain  
(childbirth; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)
- IT Headache  
Pain  
(chronic; preparation of **tricyclic spiro-oxindole** derivs. use as therapeutic agents)

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IT Nerve, disease  
(diabetic neuropathy; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Viscera  
(disease, pain; preparation of tricyclic spiro-oxindole derivs.  
use as therapeutic agents)

IT Nervous system, disease  
(dystonia, paroxysmal; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Skin, disease  
(erythroderma, familial; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Skin, disease  
(erythroderma, primary; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Pain  
(familial rectal; preparation of tricyclic spiro-oxindole derivs.  
use as therapeutic agents)

IT Muscle, disease  
(fibromyalgia; preparation of tricyclic spiro-oxindole derivs. use  
as therapeutic agents)

IT Pain  
(inflammatory pain; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Voltage-gated sodium channels  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; preparation of tricyclic spiro-oxindole derivs. use  
as therapeutic agents)

IT Pain  
(labor; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Fever and Hyperthermia  
(malignant; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Headache  
(migraine; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Neuromuscular transmission  
(myasthenia syndromes, disorders of; preparation of tricyclic  
spiro-oxindole derivs. use as therapeutic agents)

IT Muscle, disease  
(myotonia; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Bladder disease  
(neurogenic; preparation of tricyclic spiro-oxindole derivs. use  
as therapeutic agents)

IT Pain  
(neuropathic pain; preparation of tricyclic spiro-oxindole derivs.  
use as therapeutic agents)

IT Nerve, disease  
(neuropathy, HIV treatment induced; preparation of tricyclic  
spiro-oxindole derivs. use as therapeutic agents)

IT Seizures  
(partial and general tonic; preparation of tricyclic  
spiro-oxindole derivs. use as therapeutic agents)

IT Nerve, disease  
(peripheral nerve injury; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Injury  
(peripheral nerve; preparation of tricyclic spiro-oxindole derivs.

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use as therapeutic agents)

IT Pain  
(peripherally mediated; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Pain  
(persistent; preparation of tricyclic spiro-oxindole derivs. use  
as therapeutic agents)

IT Headache  
(phantom limb; preparation of tricyclic spiro-oxindole derivs. use  
as therapeutic agents)

IT Pain  
(post-surgical; preparation of tricyclic spiro-oxindole derivs.  
use as therapeutic agents)

IT Nerve, disease  
Pain  
(postherpetic neuralgia; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Amyotrophic lateral sclerosis  
Analgesics  
Antiarrhythmics  
Antiarthritics  
Anticholesteremic agents  
Anticonvulsants  
Antidepressants  
Antipsychotics  
Antirheumatic agents  
Antitumor agents  
Anxiety  
Anxiolytics  
Atherosclerosis  
Atrial fibrillation  
Bipolar disorder  
Cardiac arrhythmia  
Cardiovascular disease  
Crohn disease  
Cystic fibrosis  
Depression  
Epilepsy  
Human  
Hypercholesterolemia  
Hypothyroidism  
Irritable bowel syndrome  
Mental and behavioral disorders  
Neoplasm  
Osteoarthritis  
Pain  
Peripheral nervous system disease  
Pruritus  
Respiratory system disease  
Rheumatoid arthritis  
Schizophrenia  
Tachycardia  
Ulcerative colitis  
Ventricular fibrillation  
(preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Aldosteronism  
(pseudoaldosteronism; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Leg, disease

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Sleep disorders  
(restless leg syndrome; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Muscle, disease  
(rhabdomyolysis; preparation of tricyclic spiro-oxindole derivs.  
use as therapeutic agents)

IT Heat  
(sensitivity; preparation of tricyclic spiro-oxindole derivs. use  
as therapeutic agents)

IT Headache  
(sinus; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Disease, animal  
(sodium channel toxin related; preparation of tricyclic  
spiro-oxindole derivs. use as therapeutic agents)

IT Pain  
(surgical; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Headache  
(tension; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Pain  
(trauma; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT Nerve, disease  
Pain  
(trigeminal neuralgia; preparation of tricyclic spiro-oxindole  
derivs. use as therapeutic agents)

IT Neuroprotective agents  
(under ischemic conditions caused by stroke or neural trauma; preparation  
of  
tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Disease, animal  
(visceral pain; preparation of tricyclic spiro-oxindole derivs.  
use as therapeutic agents)

IT Pain  
(visceral; preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT 1019847-67-6P 1019847-68-7P 1019847-70-1P 1019847-71-2P  
1019847-72-3P 1019847-73-4P 1019847-74-5P 1019847-75-6P  
1019847-76-7P 1019847-77-8P 1019847-78-9P 1019847-79-0P  
1019847-80-3P  
RL: PAC (Pharmacological activity); PRPH (Prophetic); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT 1019847-61-0P 1019847-63-2P 1019847-65-4P 1019847-66-5P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)  
(preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT 533-31-3, 1,3-Benzodioxol-5-ol 7124-93-8,  
1,2,3,4,5,6-Hexahydro-1-benzazocine 7160-97-6 32281-97-3,  
7-Bromo-3,4-dihydronaphthalen-1(2H)-one 40358-33-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

IT 205584-61-8P 885953-12-8P 1019847-81-4P 1019847-82-5P

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1019847-83-6P 1019847-86-9P 1019847-87-0P 1019847-88-1P  
1019847-89-2P 1019847-91-6P 1019847-93-8P 1019847-94-9P  
1019847-95-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of tricyclic spiro-oxindole derivs. use as  
therapeutic agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 8 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:439128 ZCAPLUS Full-text

DOCUMENT NUMBER: 149:6518

TITLE: Ceramide accumulation mediates inflammation, cell  
death and infection susceptibility in cystic fibrosis

AUTHOR(S): Teichgraber, Volker; Ulrich, Martina; Endlich,  
Nicole; Riethmueller, Joachim; Wilker, Barbara; De  
Oliveira-Munding, Cheyla Conceicao; van Heeckeren,  
Anna M.; Barr, Mark L.; von Kuerthy, Gabriele; Schmid,  
Kurt W.; Weller, Michael; Tuemmler, Burkhard; Lang,  
Florian; Grassme, Heike; Doering, Gerd; Gulbins, Erich

CORPORATE SOURCE: Department of Molecular Biology, University of  
Duisburg-Essen, Essen, 45122, Germany

SOURCE: Nature Medicine (New York, NY, United States) (2008),  
14(4), 382-391

CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Microbial lung infections are the major cause of morbidity and mortality in  
the hereditary metabolic disorder cystic fibrosis, yet the mol. mechanisms  
leading from the mutation of cystic fibrosis transmembrane conductance  
regulator (CFTR) to lung infection are still unclear. Here, we show that  
ceramide age-dependently accumulates in the respiratory tract of uninfected  
Cftr-deficient mice owing to an alkalinization of intracellular vesicles in  
Cftr-deficient cells. This change in pH results in an imbalance between acid  
sphingomyelinase (Asm) cleavage of sphingomyelin to ceramide and acid  
ceramidase consumption of ceramide, resulting in the higher levels of  
ceramide. The accumulation of ceramide causes Cftr-deficient mice to suffer  
from constitutive age-dependent pulmonary inflammation, death of respiratory  
epithelial cells, deposits of DNA in bronchi and high susceptibility to severe  
Pseudomonas aeruginosa infections. Partial genetic deficiency of Asm in Cftr-  
/-Smpdl+/- mice or pharmacol. treatment of Cftr-deficient mice with the Asm  
blocker amitriptyline normalizes pulmonary ceramide and prevents all pathol.  
findings, including susceptibility to infection. These data suggest  
inhibition of Asm as a new treatment strategy for cystic fibrosis.

CC 14-4 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1

ST ceramide inflammation infection susceptibility cystic fibrosis

IT Cystic fibrosis

Human

Pneumonitis

Pseudomonas aeruginosa

Respiratory system

(ceramide accumulation mediates inflammation, cell death and infection  
susceptibility in cystic fibrosis)

IT CFTR (cystic fibrosis transmembrane  
conductance regulator)

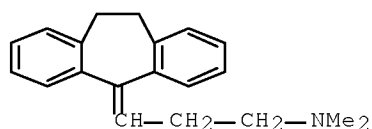
Ceramides

RL: ADV (Adverse effect, including toxicity); BSU (Biological study,



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- unclassified); BIOL (Biological study)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT Sphingomyelins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT DNA  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(deposits in respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT Respiratory system  
(epithelium, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT Apoptosis  
(of respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT Epithelium  
(respiratory tract, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT Organelle  
(vesicle, alkalinization of; ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT 57-88-5, Cholesterol, biological studies 123-78-4, Sphingosine 9031-54-3, Acid sphingomyelinase 26993-30-6, Sphingosine 1-phosphate 37289-06-8, Acid ceramidase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT 212059-03-5, Peptamen  
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT 50-48-6, Amitriptyline  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- IT 50-48-6, Amitriptyline  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in **cystic fibrosis**)
- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 9 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2007:1064527 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 147:371991  
 TITLE: Preparation and storage of stable, biologically active materials  
 INVENTOR(S): Manders, Ernest K.; Manders, Christian D.  
 PATENT ASSIGNEE(S): Promethean Lifesciences, Inc., USA  
 SOURCE: PCT Int. Appl., 25 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007106582	A2	20070920	WO 2007-US6592	20070315
WO 2007106582	A3	20071122		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			

PRIORITY APPLN. INFO.: US 2006-782420P P 20060315

AB The invention involves taking a base material such as allografts, xenografts, polymers, metals, and ceramics and combining it with a biol. active agent, such as proteins, cytokines, growth factors, and enzymes after which it is irradiated with ionizing radiation to sterilize and stabilize the material. The resulting biol. active material may then be stored at ambient temperature while maintaining its biol. activity and the structural integrity of the base material. The invention is particularly useful for eliciting desired biol. responses in human and animal medicine, and in certain industrial applications.

IC ICM A61K

CC 63-8 (Pharmaceuticals)

IT Actins

Albumins

Amyloid

Antibodies and Immunoglobulins

Barbiturates

Bone morphogenetic protein 11

Bone morphogenetic proteins

C-reactive protein

CFTR (cystic fibrosis transmembrane  
conductance regulator)

Cadherins

Chemokines

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Cholinergic receptors  
Collagens  
Cytokines  
Dystrophin  
Elastins  
Enzymes  
Eotaxins  
Estrogen receptors  
Ferritins  
Fetuin  
Fibrins  
Gelatin  
Glucose transporters  
Glycosaminoglycans  
Growth factors, animal  
Hemoglobins  
Hepatocyte growth factor  
Histones  
Hormones, animal  
Insulin receptors  
Integrins  
Interferons  
Interleukin receptors  
Interleukins  
Keratins  
Leukemia inhibitory factor  
Macrophage inflammatory protein 1 $\alpha$   
Macrophage inflammatory protein 1 $\beta$   
Macrophage inflammatory protein 3 $\beta$   
Macrophage inflammatory protein 4  
Macrophage inflammatory proteins  
Metals  
Monocyte chemoattractant proteins  
Myoglobins  
Myosins  
Neuregulin 1  
Neuregulin 1  
Peptides  
Platelet-derived growth factors  
Polymers  
Polysaccharides  
Potassium channels  
Protein C  
Proteins  
RANTES (chemokine)  
Rennets  
Selectins  
Stem cell factor  
Steroids  
T cell receptors  
Tau proteins  
Thioredoxins  
Toxins  
Toxins  
Transforming growth factors  
Tubulins  
Tumor necrosis factors  
p53 (protein)  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation and storage of stable, biol. active materials)

IT 50-06-6, Phenobarbital, biological studies 50-24-8, Prednisolone  
 50-33-9, Phenylbutazone, biological studies ~~50-48-6~~,  
 Amitriptyline 50-53-3, Chlorpromazine, biological studies 50-55-5,  
 Reserpine 50-56-6, Oxytocin, biological studies 50-78-2, Aspirin  
 51-06-9, Procainamide 51-43-4, Epinephrine 51-55-8, Atropine,  
 biological studies 57-42-1, Meperidine 57-47-6, Physostigmine  
 57-53-4, Meprobamate 58-22-0, Testosterone 58-39-9, Perphenazine  
 58-55-9, Theophylline, biological studies 58-73-1, Diphenhydramine  
 58-74-2, Papaverine 58-94-6, Chlorothiazide 59-42-7, Phenylephrine  
 59-47-2, Mephenesin 59-99-4, Neostigmine 69-23-8, Fluphenazine  
~~72-69-5~~, Nortriptyline 73-48-3, Bendroflumethiazide 76-99-3,  
 Methadone 77-21-4, Glutethimide 91-81-6, Tripeleminamine 103-90-2,  
 Acetaminophen 146-54-3, Triflupromazine 148-56-1, Flumethiazide  
 299-42-3, Ephedrine 302-17-0, Chloral hydrate 409-21-2, Silicon  
 carbide, biological studies 469-62-5, Propoxyphene 523-87-5,  
 Dimenhydrinate 525-66-6, Propranolol 1302-88-1, Cordierite  
 1314-23-4, Zirconia, biological studies 1344-28-1, Alumina, biological  
 studies 1398-61-4, Chitin 5818-17-7, Methantheline 7440-06-4,  
 Platinum, biological studies 7440-09-7, Potassium, biological studies  
 7440-22-4, Silver, biological studies 7440-32-6, Titanium, biological  
 studies 7440-57-5, Gold, biological studies 7632-10-2, Deoxyephedrine  
 9000-69-5, Pectin 9000-83-3, ATPase 9000-86-6, Alanine transaminase  
 9000-92-4, Amylase 9000-96-8, Arginase 9000-97-9 9001-03-0, Carbonic  
 anhydrase 9001-05-2, Catalase 9001-06-3, Chitinase 9001-08-5,  
 Cholinesterase 9001-15-4, Creatine kinase 9001-16-5, Cytochrome c  
 oxidase 9001-25-6, Blood-coagulation factor VII 9001-28-9, Factor IX  
 9001-29-0, Blood-coagulation factor X 9001-30-3, Blood-coagulation  
 factor XII 9001-37-0, Glucose oxidase 9001-42-7, Maltase 9001-48-3,  
 Glutathione reductase 9001-50-7, Glyceraldehyde 3-phosphate  
 dehydrogenase 9001-51-8, Hexokinase 9001-52-9, Fructose biphosphatase  
 9001-54-1, Hyaluronidase 9001-58-5, Isocitrate dehydrogenase  
 9001-60-9, Lactate dehydrogenase 9001-63-2, Lysozyme 9001-64-3, Malate  
 dehydrogenase 9001-66-5, Monoamine oxidase 9001-69-8, Ornithine  
 trans-carbamoylase 9001-75-6, Pepsin 9001-78-9, Alkaline phosphatase  
 9001-80-3, Phosphofructokinase 9001-81-4, Phosphoglucomutase  
 9001-90-5, Plasmin 9001-99-4 9002-03-3, Dihydrofolate reductase  
 9002-04-4, Thrombin 9002-06-6, Thymidine kinase 9002-07-7, Trypsin  
 9002-08-8, Thrombinogen 9002-10-2, Catechol oxidase 9002-12-4, Urate  
 oxidase 9002-13-5, Urease 9002-17-9, Xanthine oxidase 9003-98-9,  
 Deoxyribonuclease 9003-99-0, Myeloperoxidase 9004-02-8, Lipoprotein  
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 Insulin, biological studies 9004-32-4, Carboxymethyl cellulose  
 9004-57-3, Ethyl cellulose 9004-62-0, Hydroxyethyl cellulose  
 9004-64-2, Hydroxypropyl cellulose 9005-38-3, Algin 9005-49-6,  
 Heparin, biological studies 9012-25-3, Catechol-O-methyl transferase  
 9012-42-4, Adenylate cyclase 9012-49-1, Aspartate transcarbamoylase  
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 DNA polymerase 9013-02-9, Adenylate kinase 9013-04-1, Nitrogenase  
 9013-55-2, Blood-coagulation factor XI 9013-56-3, Factor XIII  
 9013-66-5, Glutathione peroxidase 9013-93-8, Phospholipase 9014-19-1,  
 Pyruvate carboxylase 9014-20-4, Pyruvate dehydrogenase 9014-42-0,  
 Thrombopoietin 9014-52-2, Tryptophan synthase 9015-82-1,  
 Angiotensin-converting enzyme 9015-94-5, Renin, biological studies  
 9016-11-9, Galactose-1-phosphate uridylyltransferase 9016-12-0,  
 Hypoxanthine-guanine phosphoribosyltransferase 9023-56-7, CTP synthase  
 9023-58-9, Argininosuccinate synthetase 9023-93-2, Acetyl-CoA  
 carboxylase 9024-60-6, Ornithine decarboxylase 9024-78-6, Kynureninase  
 9024-90-2, Nitrilase 9026-81-7, Nuclease 9026-93-1, Adenosine  
 deaminase 9027-03-6, Coenzyme Q-cytochrome c reductase 9027-23-0,

RubisCO 9027-41-2, Hydrolase 9028-13-1, Homoserine dehydrogenase 9028-14-2, Glycerol dehydrogenase 9028-15-3, Propanediol phosphate dehydrogenase 9028-16-4, D-Xylulose reductase 9028-17-5, L-Xylulose reductase 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase 9028-49-3, Diacetyl reductase 9028-69-7, Methylenetetrahydrofolate reductase 9028-78-8, L-Gulonolactone oxidase 9028-86-8, Acetaldehyde dehydrogenase 9029-22-5, Sarcosine oxidase 9029-38-3, Sulfite oxidase 9029-53-2, Cytochrome c peroxidase 9029-72-5, 4-Hydroxyphenylpyruvate dioxygenase 9029-73-6, Phenylalanine hydroxylase 9030-23-3, Platelet derived endothelial cell growth factor 9030-35-7, Thiaminase 9031-11-2, Lactase 9031-28-1, Thyroid peroxidase 9031-37-2, Ceruloplasmin 9031-44-1, Kinase (phosphorylating) 9031-72-5, Alcohol dehydrogenase 9034-39-3, Growth Hormone Releasing Factor 9035-82-9, Dehydrogenase 9037-14-3, Aminolevulinic acid synthase 9037-42-7 9039-48-9, Aromatase 9042-64-2, Aromatic-L-amino acid decarboxylase 9046-27-9 9046-38-2, Polygalacturonic acid 9054-63-1, Alanine aminopeptidase 9054-75-5, Guanylate cyclase 9054-89-1, Superoxide dismutase 9055-11-2 9057-02-7, Pullulan 9061-61-4, Nerve growth factor 9067-75-8, Blood-coagulation factor XIIIa 9068-38-6, Reverse transcriptase 9068-57-9, Acrosin 9073-60-3 9074-10-6, Biliverdin reductase 9074-14-0, Thioredoxin reductase 9075-08-5 9075-42-7, Cytochrome P450 oxidase 9075-65-4, Glycerol-3-phosphate dehydrogenase 9076-80-6 9079-67-8 9081-34-9, 5- $\alpha$  Reductase 11096-26-7, Erythropoietin 11100-70-2, Vanadium steel, biological studies 12033-89-5, Silicon nitride, biological studies 12597-68-1, Stainless steel, biological studies 12683-48-6 14378-12-2, Steatite 25249-06-3, Polygalacturonic acid 37205-63-3, ATP synthase 37228-74-3 37250-13-8 37259-58-8 37270-94-3, Platelet factor 4 37288-39-4 37289-19-3, GTP cyclohydrolase I 37318-49-3, Protein disulfide isomerase 42200-33-9, Nadolol 49557-75-7 50812-37-8, Glutathione S-transferase 52013-44-2 53986-32-6, Protoporphyrinogen oxidase 57285-09-3, Inhibin 60202-16-6, Protein C 61869-41-8, Renilla luciferase 61912-98-9, Insulin-like growth factor 61969-99-1, Cypridina luciferase 61970-00-1, Firefly luciferase 62031-54-3, Fibroblast growth factor 62213-29-0 62229-50-9, Epidermal growth factor 62571-86-2, Captopril 62683-29-8, Colony-stimulating factor 63774-49-2 64885-96-7, Primase 72103-04-9, Deiodinase 73200-91-6, DMSO reductase 74870-74-9, Uridine monophosphate synthase 75847-73-3, Enalapril 80449-02-1 80498-15-3, Laccase 81669-70-7 86480-67-3, Ubiquitin carboxyterminal hydrolase 106956-32-5, Oncostatin M 114051-83-1, Dihydrobenzophenanthridine oxidase 117147-70-3, Amphiregulin 125978-95-2 127464-60-2, Vascular endothelial growth factor 139639-23-9, Tissue plasminogen activator 141907-41-7 142008-29-5, CAMP-dependent protein kinase 148348-15-6, Fibroblast growth factor 7 154531-34-7, HB-EGF 154947-66-7, LL-37 163150-12-7, Betacellulin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation and storage of stable, biol. active materials)

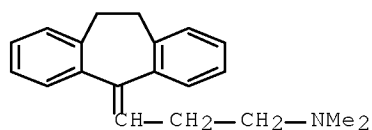
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation and storage of stable, biol. active materials)

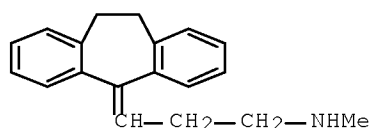
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CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)

10/524815



RN 72-69-5 ZCAPLUS  
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



L91 ANSWER 10 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2006:605195 ZCAPLUS Full-text  
DOCUMENT NUMBER: 145:83360  
TITLE: Novel heterocyclic compounds, their preparation, and their use as PDE4 inhibitors for treating inflammatory and allergic disorders  
INVENTOR(S): Gharat, Laxmikant Atmaram; Gopalan, Balasubramanian; Khairatkar-Joshi, Neelima  
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals S.A., Switz.  
SOURCE: PCT Int. Appl., 145 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2006064355	A2	20060622	WO 2005-IB3798	20051215
WO 2006064355	A3	20060803		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2005315319	A1	20060622	AU 2005-315319	20051215
CA 2591438	A1	20060622	CA 2005-2591438	20051215
EP 1831227	A2	20070912	EP 2005-826587	20051215

10/524815

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
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BA, HR, MK, YU

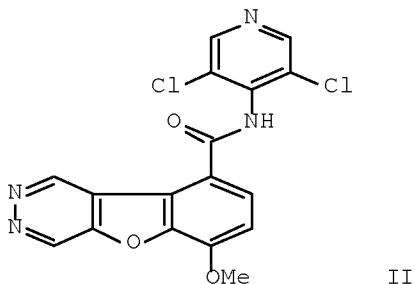
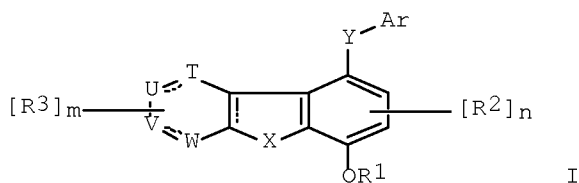
JP 2008524201	T	20080710	JP 2007-546221	20051215
BR 2005017211	A	20080930	BR 2005-17211	20051215
MX 2007007345	A	20070907	MX 2007-7345	20070618
KR 2007100254	A	20071010	KR 2007-714219	20070622
NO 2007003436	A	20070905	NO 2007-3436	20070703
ZA 2007006097	A	20080730	ZA 2007-6097	20070713
IN 2007MN01058	A	20090522	IN 2007-MN1058	20070713
CN 101124229	A	20080213	CN 2005-80048315	20070814

PRIORITY APPLN. INFO.:

IN 2004-MU1352	A	20041217
US 2004-637232P	P	20041217
WO 2005-IB3798	W	20051215

OTHER SOURCE(S): CASREACT 145:83360; MARPAT 145:83360

GI



AB The invention is related to novel phosphodiesterase type 4 (PDE4) inhibitors of the formula I [R1-R3 at each occurrence = independently H, OH, CN, halo, (un)substituted alk(en/yn)yl, hetero/aryl, NH<sub>2</sub> and derivs., etc.; Ar = (un)substituted hetero/aryl, hetero/arylalkyl, heterocyclyl, heterocycloalkyl; m = 0-8; n = 0-2; T, U, V, W = independently C, C:O, N, NH and derivs., O, S, with the proviso that at least one of T, U, V, and W are N, NH and derivs., O, or S; X = O, S, SO, SO<sub>2</sub>, NH and derivs.; Y = CONH and derivs., NHSO<sub>2</sub> and derivs., SO<sub>2</sub>NH and derivs., NHCO, and derivs.] and analogs, tautomers, enantiomers, diastereomers, regioisomers, stereoisomers, polymorphs, pharmaceutically acceptable salts, N-oxides, pharmaceutically acceptable solvates thereof, their preparation, and the pharmaceutical compns. containing them which are useful in the treatment of allergic (no data), inflammatory (no data), central nervous system diseases (no data) and insulin-resistant diabetes (no data). For example, II was prepared in 13 steps via cyclization of 2-Et 4-Me 3-formyl-7-methylbenzo[b]furan-2,4-dicarboxylate with hydrazine hydrate, followed by aromatization with POCl<sub>3</sub> to 4-chlorobenzofuropyrizidine derivative, dechlorination, saponification of the ester, esterification with p-nitrophenol, and reaction with 4-amino-3,5-dichloropyridine. II inhibited the PDE4-induced conversion of [3H]cAMP to the corresponding [3H]5'-AMP with IC<sub>50</sub> of 1.375 nM. Thus, I and their compns., are useful for treating

- including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and reperfusion injury of the brain, chronic glomerulonephritis, endotoxic shock, adult respiratory distress syndrome, etc. (no data).
- CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63
- IT Tumor necrosis factors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(1, secretion; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation  
(Crohn's disease; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Intestine, disease  
(Crohn's; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Respiratory distress syndrome  
(adult; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Allergy  
Eye, disease  
Inflammation  
(allergic conjunctivitis; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Allergy  
Inflammation  
Nose, disease  
(allergic rhinitis; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Dermatitis  
(atopic; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Muscle  
(cardiac, reperfusion injury of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Brain, disease  
(cerebrovascular; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Bronchi, disease  
Inflammation  
(chronic bronchitis; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation  
Kidney, disease  
(chronic glomerulonephritis; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Lung, disease



- (chronic obstructive pulmonary disease; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation  
(chronic; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Eye, disease  
Inflammation  
(conjunctivitis, adult vernal; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Mental and behavioral disorders  
(dementia; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Mental and behavioral disorders  
(depression; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Granuloma  
(eosinophilic; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Heart, disease  
(failure; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Eye  
Heart  
Intestine  
Joint, anatomical  
Lung  
Skin  
(inflammatory condition or immune disorder of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Intestine, disease  
(inflammatory; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Reperfusion  
(injury, of myocardium and brain; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Diabetes mellitus  
(insulin-resistant; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Heart  
(myocardium, reperfusion injury of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation  
Kidney, disease  
(nephritis; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Allergy

Allergy inhibitors  
 Alzheimer's disease  
 Amnesia  
 Anti-Alzheimer's agents  
 Anti-inflammatory agents  
 Antiarthritics  
 Antiasthmatics  
   Antidepressants  
 Antidiabetic agents  
 Antirheumatic agents  
 Asthma  
 Bronchodilators  
 Cardiovascular agents  
 Central nervous system, disease  
 Central nervous system agents  
   Cystic fibrosis  
 Drug delivery systems  
 Eczema  
 Gout  
 Human  
 Immune disease  
 Immunomodulators  
 Inflammation  
 Multiple sclerosis  
 Osteoarthritis  
 Psoriasis  
 Psychotropics  
 Respiratory distress syndrome  
 Rheumatic diseases  
 Shock (circulatory collapse)  
 Urticaria

(preparation of **tricyclic** heterocycles as PDE4 inhibitors for  
 treating inflammatory, immune and central nervous system disorders, and  
 insulin-resistant diabetes)

# IT Tricyclic compounds

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of **tricyclic** heterocycles as PDE4 inhibitors for  
 treating inflammatory, immune and central nervous system disorders, and  
 insulin-resistant diabetes)

# IT Brain

(reperfusion injury of; preparation of **tricyclic** heterocycles as  
 PDE4 inhibitors for treating inflammatory, immune and central nervous  
 system disorders, and insulin-resistant diabetes)

# IT Injury

(reperfusion, of myocardium and brain; preparation of **tricyclic**  
 heterocycles as PDE4 inhibitors for treating inflammatory, immune and  
 central nervous system disorders, and insulin-resistant diabetes)

# IT Shock (circulatory collapse)

(septic; preparation of **tricyclic** heterocycles as PDE4 inhibitors  
 for treating inflammatory, immune and central nervous system disorders,  
 and insulin-resistant diabetes)

# IT Inflammation

Spinal column, disease

(spondylitis, rheumatoid; preparation of **tricyclic** heterocycles as  
 PDE4 inhibitors for treating inflammatory, immune and central nervous  
 system disorders, and insulin-resistant diabetes)

# IT Inflammation

Intestine, disease

- (ulcerative colitis; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Eye, disease  
Inflammation  
(uveitis; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 893554-81-9P 893555-11-8P 893555-23-2P 893555-31-2P 893555-43-6P, tert-Butyl 9-[(3,5-dichloropyridin-4-yl)carbamoyl]-6-methoxy-5-methyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-51-6P 893555-74-3P 893555-90-3P  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(drug candidate; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 893554-92-2P 893554-99-9P 893555-22-1P 893555-34-5P 893555-35-6P 893555-49-2P, tert-Butyl 9-[(3,5-dichloropyridin-4-yl)carbamoyl]-6-methoxy-5-benzyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-50-5P, tert-Butyl 9-[(3,5-dichloropyridin-4-yl)carbamoyl]-6-methoxy-5-cyclopropylmethyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-52-7P 893555-53-8P 893555-54-9P 893555-55-0P, tert-Butyl 9-[(pyridin-4-yl)carbamoyl]-6-methoxy-5-methyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-56-1P 893555-57-2P 893555-61-8P 893555-64-1P 893555-68-5P 893555-88-9P 893555-89-0P 893555-91-4P 893555-92-5P 893555-96-9P 893556-00-8P 893556-04-2P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(drug candidate; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 9036-21-9, PDE4  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(insulin-resistant diabetes; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 18703-79-2P, Ethyl 2-(2-methoxyphenoxy)-3-oxobutanoate 18703-82-7P, Ethyl 7-methoxy-3-methylbenzo[b]furan-2-carboxylate 29025-30-7P, 7-Methoxy-2-methylbenzo[b]furan 39581-47-0P, (7-Methoxybenzo[b]furan-3-yl)acetonitrile 41580-71-6P, 1-Methoxy-2-(2-propynyloxy)benzene 50551-58-1P 70076-67-4P, Ethyl 2-(2-formyl-6-methoxyphenoxy)acetate 75566-54-0P, (7-Methoxybenzo[b]furan-2-yl)methanol 75566-55-1P, 2-(Chloromethyl)-7-methoxy-1-benzofuran 75566-56-2P, (7-Methoxybenzo[b]furan-2-yl)acetonitrile 91872-02-5P, 4-Amino-3,5-dichloropyridine N-oxide 130627-28-0P, 7-Methoxy-2-methylbenzo[b]furan-4-carboxaldehyde 203575-64-8P, 7-Methoxy-2-methylbenzo[b]furan-4-carboxylic acid 206761-96-8P, Ethyl 4-[(2-methoxyphenyl)sulfanyl]-3-oxobutanoate 893554-82-0P, Ethyl 4-formyl-7-methoxy-3-methylbenzo[b]furan-2-carboxylate 893554-83-1P, 2-Ethoxycarbonyl-7-methoxy-3-methylbenzo[b]furan-4-carboxylic acid

893554-84-2P 893554-85-3P 893554-86-4P 893554-87-5P 893554-88-6P  
 893554-89-7P 893554-90-0P 893554-91-1P 893554-93-3P, Ethyl  
 2-(2-cyano-6-methoxyphenoxy)acetate 893554-94-4P 893554-95-5P  
 893554-96-6P 893554-97-7P 893554-98-8P 893555-00-5P, Methyl  
 7-methoxy-2-methylbenzo[b]furan-4-carboxylate 893555-01-6P, Methyl  
 2-bromomethyl-7-methoxybenzo[b]furan-4-carboxylate 893555-02-7P, Methyl  
 2-formyl-7-methoxybenzo[b]furan-4-carboxylate 893555-03-8P,  
 (Z)-3-[7-Methoxy-4-[(methyloxy)carbonyl]benzo[b]furan-2-yl]-2-propenoic  
 acid 893555-04-9P, Methyl 2-[(Z)-2-(azidocarbonyl)ethenyl]-7-  
 methoxybenzo[b]furan-4-carboxylate 893555-05-0P 893555-06-1P  
 893555-07-2P 893555-08-3P 893555-09-4P 893555-10-7P 893555-12-9P,  
 2-Ethoxycarbonyl-7-hydroxy-3-methylbenzo[b]furan-4-carboxylic acid  
 893555-13-0P 893555-14-1P 893555-15-2P, Diethyl  
 3-bromomethyl-7-difluoromethoxybenzo[b]furan-2,4-dicarboxylate  
 893555-16-3P, Diethyl 7-difluoromethoxy-3-formylbenzo[b]furan-2,4-  
 dicarboxylate 893555-17-4P 893555-18-5P 893555-19-6P 893555-20-9P  
 893555-21-0P 893555-24-3P, Ethyl  
 2-(7-methoxybenzo[b]thiophen-3-yl)acetate 893555-25-4P,  
 2-(7-Methoxybenzo[b]thiophen-3-yl)acetamide 893555-26-5P,  
 [2-(7-Methoxybenzo[b]thiophen-3-yl)ethyl]amine 893555-27-6P, Ethyl  
 [2-(7-methoxybenzo[b]thiophen-3-yl)ethyl]carbamate 893555-32-3P  
 893555-33-4P 893555-36-7P, 2-(7-Methoxybenzo[b]furan-2-yl)ethanamine  
 893555-37-8P, Ethyl [2-(7-methoxybenzo[b]furan-2-yl)ethyl]carbamate  
 893555-38-9P 893555-39-0P 893555-40-3P 893555-41-4P 893555-42-5P  
 893555-44-7P, Methyl 3-(2-chlorohydrazino)-4-methoxybenzoate  
 893555-45-8P 893555-46-9P 893555-47-0P,  
 2-(tert-Butyloxycarbonyl)-6-methoxy-5-methyl-1,3,4,5-tetrahydro-2H-  
 pyrido[4,3-b]indole-9-carboxylic acid 893555-48-1P 893555-58-3P,  
 2-(7-Methoxybenzo[b]furan-3-yl)ethanamine hydrochloride 893555-59-4P,  
 Ethyl [2-(7-methoxybenzo[b]furan-3-yl)ethyl]carbamate 893555-60-7P  
 893555-62-9P 893555-63-0P 893555-65-2P 893555-66-3P 893555-67-4P  
 893555-69-6P 893555-70-9P 893555-71-0P 893555-72-1P 893555-73-2P  
 893555-75-4P, 7-Hydroxy-2-methylbenzo[b]furan-4-carboxaldehyde  
 893555-76-5P, 7-Cyclopentyloxy-2-methylbenzo[b]furan-4-carboxaldehyde  
 893555-77-6P, 7-Cyclopentyloxy-2-methylbenzo[b]furan-4-carboxylic acid  
 893555-78-7P, Methyl 7-cyclopentyloxy-2-methylbenzo[b]furan-4-carboxylate  
 893555-79-8P, Methyl 7-cyclopentyloxy-2-bromomethylbenzo[b]furan-4-  
 carboxylate 893555-80-1P, Methyl  
 2-formyl-7-(cyclopentyloxy)benzo[b]furan-4-carboxylate 893555-81-2P,  
 (Z)-3-[7-Cyclopentyloxy-4-[(methyloxy)carbonyl]benzo[b]furan-2-yl]-2-  
 propenoic acid 893555-82-3P 893555-83-4P 893555-84-5P 893555-85-6P  
 893555-86-7P 893555-87-8P 893555-93-6P 893555-94-7P 893555-95-8P  
 893555-97-0P 893555-98-1P 893555-99-2P 893556-01-9P 893556-02-0P  
 893556-03-1P 893556-05-3P 893556-06-4P 893556-07-5P 893556-08-6P  
 1097718-39-2P 1097721-21-5P 1097721-58-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(intermediate; preparation of ~~tricyclic~~ heterocycles as PDE4  
 inhibitors for treating inflammatory, immune and central nervous system  
 disorders, and insulin-resistant diabetes)

IT 90-05-1, Guaiacol 100-02-7, p-Nitrophenol, reactions 105-36-2, Ethyl  
 bromoacetate 106-96-7, Propargyl bromide 109-65-9, n-Butyl bromide  
 137-43-9, Cyclopentyl bromide 148-53-8, o-Vanillin 372-09-8,  
 Cyanoacetic acid 504-24-5, 4-Aminopyridine 621-59-0, Isovanillin  
 638-07-3, Ethyl 4-chloroacetoacetate 1073-70-7, p-Chlorophenylhydrazine  
 hydrochloride 3731-16-6, 3-Carbethoxy-2-piperidone 7051-34-5,  
 Cyclopropylmethyl bromide 7169-37-1, 7-Methoxy-1-benzofuran-3(2H)-one  
 7217-59-6 22889-78-7, 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl  
 4-methoxy-3-aminobenzoate 54527-68-3, 2-Chloroethyl acetoacetate  
 79099-07-3, N-Boc-4-piperidone

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RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for  
treating inflammatory, immune and central nervous system disorders, and  
insulin-resistant diabetes)

IT 1027054-25-6P 1097710-58-1P 1097711-07-3P 1108149-13-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for  
treating inflammatory, immune and central nervous system disorders, and  
insulin-resistant diabetes)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 11 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:318526 ZCAPLUS Full-text

DOCUMENT NUMBER: 144:344946

TITLE: Molecular toxicity models based on gene expression  
profiles in isolated rat hepatocytes exposed to known  
hepatotoxins

INVENTOR(S): Higgs, Brandon; Elashoff, Michael; Mendrick, Donna L.;  
Porter, Mark W.; Castle, Arthur L.; Johnson, Kory R.

PATENT ASSIGNEE(S): Gene Logic, Inc., USA

SOURCE: PCT Int. Appl., 271 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2006037025	A2	20060406	WO 2005-US34780	20050928
WO 2006037025	A3	20060713		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2004-613292P P 20040928

AB The present invention includes methods of predicting hepatotoxicity of test  
agents and methods of generating hepatotoxicity prediction models using  
algorithms for analyzing quant. gene expression information. Isolated Sprague-  
Dawley rat hepatocytes exposed to known hepatotoxins were examined to identify  
changes in genes expression induced by these compds. using the Affymetrix Rat  
Microarray. These changes in gene expression provide useful toxicity markers  
than can be used to monitor toxicity and/or toxicity progression by a test  
compound Some of these markers may also be used to monitor or detect various  
disease or physiol. states, disease progression, drug efficacy, and drug  
metabolism The invention also includes microarrays, computer systems  
comprising the toxicity prediction models, as well as methods of using the  
computer systems by remote users for determining the toxicity of test agents.

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CC 4-3 (Toxicology)  
Section cross-reference(s): 3

IT APC protein  
Agrins  
Bone morphogenetic protein 6  
C-reactive protein  
CD3 (antigen)  
CD59 (antigen)  
CFTR (cystic fibrosis transmembrane  
conductance regulator)  
Calcitonin gene-related peptide receptors  
Calnexin  
Fibronectins  
GAP-43 (protein)  
Glucagon receptors  
Gonadotropin receptors  
Growth hormone receptors  
Haptoglobin  
Hemopexins  
Insulin receptors  
Interleukin 15  
Interleukin 4 receptors  
Interleukin 6 receptors  
Intrinsic factors  
Leukemia inhibitory factor receptors  
Macrophage inflammatory protein 1 $\alpha$   
Metallothioneins  
Neuregulin 1  
Nicotinic receptors  
Polymeric immunoglobulin receptors  
TCR (T cell receptors)  
Tau factor  
Transferrin receptors  
Transferrins  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(mol. toxicity models based on gene expression profiles in isolated rat  
hepatocytes exposed to known hepatotoxins)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies  
~~50-48-6~~, Amitriptyline 50-78-2, Acetylsalicylic acid 51-61-6,  
Dopamine, biological studies 53-86-1, Indomethacin 54-85-3, Isoniazid  
55-18-5, Diethylnitrosamine 56-23-5, Carbon tetrachloride, biological  
studies 56-49-5, 3-Methylcholanthrene 57-47-6, Physostigmine  
57-63-6, 17 $\alpha$ -Ethinylestradiol 57-92-1, Streptomycin, biological  
studies 58-73-1, Diphenhydramine 59-05-2, Methotrexate 60-54-8,  
Tetracycline 62-44-2, Phenacetin 62-55-5, Thioacetamide 62-75-9,  
Dimethylnitrosamine 67-66-3, Chloroform, biological studies 99-66-1  
103-90-2, Acetaminophen 107-18-6, Allyl alcohol, biological studies  
108-86-1, Bromobenzene, biological studies 113-92-8, Chlorpheniramine  
maleate 298-46-4, Carbamazepine 321-64-2, Tacrine 427-51-0,  
Cyproterone acetate 551-06-4, 1-Naphthyl isothiocyanate 637-07-0,  
Clofibrate 657-24-9, Metformin 1403-66-3, Gentamicin 1951-25-3,  
Amiodarone 2764-72-9, Diquat 6621-47-2 7778-39-4, Arsenic acid  
10540-29-1, Tamoxifen 13073-35-3, L-Ethionine 13311-84-7, Flutamide  
15307-86-5, Diclofenac 22494-42-4, Diflunisal 25122-41-2, Clobetasol  
25451-15-4, Felbamate 25812-30-0, Gemfibrozil 29342-05-0, Ciclopirox  
33419-42-0, Etoposide 37148-27-9, Clenbuterol 49562-28-9, Fenofibrate  
49780-10-1, AY-25329 50892-23-4 52214-84-3, Ciprofibrate 75330-75-5,  
Lovastatin 122320-73-4, Rosiglitazone 132138-76-2, CI 1000  
393186-10-2, Compound A

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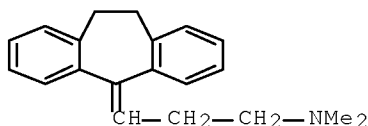
RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(mol. toxicity models based on gene expression profiles in isolated rat hepatocytes exposed to known hepatotoxins)

IT 50-48-6, Amitriptyline

RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(mol. toxicity models based on gene expression profiles in isolated rat hepatocytes exposed to known hepatotoxins)

RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



L91 ANSWER 12 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:823681 ZCAPLUS Full-text

DOCUMENT NUMBER: 143:216704

TITLE: Crystalline polymorphs of a CXC-chemokine receptor ligand

INVENTOR(S): Hu, Mengwei; Yu, Younong; Dwyer, Michael; Taveras, Arthur G.; Kim-Meade, Agnes; Yin, Jianguo; Fu, Xiaoyong; Mcallister, Timothy; Zhang, Shuyi; Klopfer, Kevin

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075447	A1	20050818	WO 2005-US3414	20050128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005210504	A1	20050818	AU 2005-210504	20050128
AU 2005210504	B2	20090108		
CA 2554709	A1	20050818	CA 2005-2554709	20050128
US 20050192345	A1	20050901	US 2005-45772	20050128
EP 1723131	A1	20061122	EP 2005-712748	20050128

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R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA,  
HR, LV, MK, YU

CN 1914187	A	20070214	CN 2005-80003507	20050128
BR 2005007329	A	20070703	BR 2005-7329	20050128
JP 2007519751	T	20070719	JP 2006-551613	20050128
MX 2006008599	A	20060828	MX 2006-8599	20060728
KR 2006128981	A	20061214	KR 2006-715429	20060728
KR 883476	B1	20090216		
IN 2006CN02800	A	20070608	IN 2006-CN2800	20060728
ZA 2006006295	A	20080227	ZA 2006-6295	20060728
NO 2006003841	A	20061027	NO 2006-3841	20060829
US 20080279822	A1	20081113	US 2008-174470	20080716

PRIORITY APPLN. INFO.:

US 2004-540487P	P	20040130
US 2005-45772	A1	20050128
WO 2005-US3414	W	20050128

AB The present invention relates to 4 distinct crystalline polymorphs of a monohydrate of 2-hydroxy-N,N-dimethyl-3-[[2-[[1-(5-methyl-2-furanyl)propyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]amino]benzamide. These 4 polymorphic forms, herein referred to as Forms I, II, III and IV are active as a CXC-chemokine receptor ligands. The invention is further directed to formulations, methods of treatment, and processes of synthesis of these polymorphic forms.

IC ICM C07D307-52  
ICS A61K031-341; A61P029-00; A61P035-00

CC 63-6 (Pharmaceuticals)

IT Acne  
Alzheimer's disease  
Angiogenesis  
Angiogenesis inhibitors  
Anticoagulants  
Anticonvulsants  
Antidepressants  
Antirheumatic agents  
Antitumor agents  
Arthritis  
Asthma  
Atherosclerosis  
Autoimmune disease  
Bronchodilators  
Burn  
Celiac disease  
Common cold  
Cough  
Cystic fibrosis  
Decongestants  
Dopamine agonists  
Drug delivery systems  
Dyspnea  
Emphysema  
Encephalitis  
Expectorants  
Gout  
Hemorrhage  
Hepatitis virus  
Human  
Human herpesvirus  
Human immunodeficiency virus 1  
Hypercapnia  
Immunosuppressants



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Inflammation  
Ischemia  
Leukotriene antagonists  
Lupus erythematosus  
Malaria  
Meningitis  
Multiple sclerosis  
Neoplasm  
Osteoarthritis  
Osteoporosis  
Pain  
Parturition  
Platelet aggregation inhibitors  
Polymorphism (crystal)  
Pruritus  
Psoriasis  
Rheumatoid arthritis  
Sarcoidosis  
Sepsis  
Strain  
Thrombolytics  
Thrombosis

$\beta$ 2-Adrenoceptor agonists

Natural products, pharmaceutical

RL: BIOL (Biological study); USES (Uses)

(crystalline polymorphs of CXC-chemokine receptor ligand)

IT 50-48-6 53-03-2, Prednisone 53-86-1, Indomethacin 59-05-2,  
Methotrexate 72-69-5 298-46-4, Carbamazepin 378-44-9,  
Betamethasone 446-86-6 599-79-1, Sulfasalazine 9005-49-6, Heparin,  
biological studies 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen  
22204-53-1, Naproxen 36322-90-4, Piroxicam 60142-96-3, Gabapentin  
65271-80-9 71125-38-7, Meloxicam 75706-12-6, Leflunimide 79217-60-0,  
Cyclosporin 84057-84-1, Lamotrigine 105857-23-6, Alteplase  
139639-23-9, Tissue plasminogen activator 143653-53-6, Abciximab  
147245-92-9, Glatiramer acetate 148553-50-8, PreGabaline 162011-90-7,  
Rofecoxib 169590-42-5, Celecoxib 170277-31-3, Infliximab  
181695-72-7, Valdecoxib 185243-69-0, Etanercept 188627-80-7,  
Eftifibatide 191588-94-0, Tenecteplase 202409-33-4, Etoricoxib  
331731-18-1, Adalimumab

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crystalline polymorphs of CXC-chemokine receptor ligand)

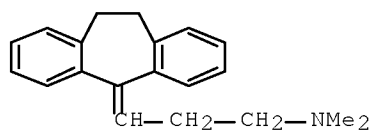
IT 50-48-6 72-69-5

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crystalline polymorphs of CXC-chemokine receptor ligand)

RN 50-48-6 ZCAPLUS

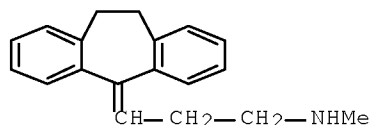
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-  
dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS

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CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)  
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 13 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:673292 ZCAPLUS Full-text  
DOCUMENT NUMBER: 143:172866  
TITLE: Preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands  
INVENTOR(S): Taveras, Arthur G.; Zheng, Junying; Biju, Purakkattle J.; Yu, Younong; Chao, Jianhua; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.; Lai, Gaifa; Wu, Minglang  
PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.  
SOURCE: PCT Int. Appl., 427 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005068460	A1	20050728	WO 2004-US42720	20041220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2550540	A1	20050728	CA 2004-2550540	20041220
US 20060025453	A1	20060202	US 2004-17505	20041220
EP 1697354	A1	20060906	EP 2004-814856	20041220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1918156	A	20070221	CN 2004-80041794	20041220
JP 2007515489	T	20070614	JP 2006-547206	20041220
MX 2006007205	A	20060831	MX 2006-7205	20060622
PRIORITY APPLN. INFO.:			US 2003-531693P	P 20031222

OTHER SOURCE(S): CASREACT 143:172866; MARPAT 143:172866  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Disclosed are novel compds. I [D, E = N, CR50; provided that D and E are not the same (one is N and the other is CR50); R50 = H, CF3, CN, etc.; A = (hetero)aryl, (hetero)arylalkyl; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and cardiac reperfusion injury, pain (e.g., acute pain, acute and chronic inflammatory pain, and neuropathic pain) using a compound I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 68% yield from the isothiazoledioxide III and the amine IV.pTSA (preparation of reactants given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

IC ICM C07D417-12  
ICS C07D275-02; C07D417-14; A61K031-427; A61P035-00; A61P029-00

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

IT AIDS (disease)  
Acne  
Alzheimer's disease  
Analgesics  
Anemia (disease)  
Angiogenesis  
Angiogenesis inhibitors  
Anti-AIDS agents  
Anti-Alzheimer's agents  
Anti-ischemic agents  
Antianginal agents  
Antiarthritics  
Antiasthmatics  
Antidiabetic agents  
Antimalarials  
Antiphospholipid syndrome  
Antirheumatic agents  
Antitumor agents  
Antitussives  
Antiulcer agents  
Antiviral agents  
Arthritis  
Asthma  
Atherosclerosis  
Behcet's syndrome  
Burn  
Celiac disease  
Central nervous system, neoplasm  
Cirrhosis  
Combination chemotherapy  
Common cold  
Cough  
Cystic fibrosis  
Dermatomyositis

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Diabetes mellitus  
Drug delivery systems  
Dyspnea  
Emphysema  
Encephalitis  
Fibrosis  
Gout  
Graves' disease  
Hepatitis virus  
Herpesviridae  
Human  
Human herpesvirus  
Human herpesvirus 8  
Hypercapnia  
Hypoxia  
Immunomodulators  
Lung, disease  
Lupus erythematosus  
Malaria  
Meningitis  
Multiple organ failure  
Multiple sclerosis  
Myasthenia gravis  
Myelodysplastic syndromes  
Myositis  
Neoplasm  
Osteoarthritis  
Osteoporosis  
Pruritus  
Psoriasis  
Respiratory system, disease  
Rheumatoid arthritis  
Sarcoidosis  
Sjogren syndrome  
Thrombosis  
Vitiligo

(preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands)

IT 50-18-0, Cyclophosphamide 50-48-6, Amitriptyline 51-21-8,  
5-Fluorouracil 53-03-2, Prednisone 53-86-1, Indomethacin 57-22-7,  
Vincristine 59-05-2, Methotrexate 72-69-5, Nortriptyline  
298-46-4, Carbamazepine 378-44-9,  $\beta$ -Methasone 446-86-6,  
Azothioprine 599-79-1, Sulfasalazine 9005-49-6, Heparin, biological  
studies 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22204-53-1,  
Naproxen 33069-62-4, Paclitaxel 36322-90-4, Piroxicam 60142-96-3,  
Gabapentin 65271-80-9, Mitoxantrone 75706-12-6, Leflunomide  
79217-60-0, Cyclosporin 84057-84-1, Lamotrigine 85622-93-1,  
Temozolomide 95058-81-4, Gemcitabine 105857-23-6, Alteplase  
143653-53-6, Abciximab 147245-92-9, Glatiramer acetate 148553-50-8,  
Pregabalin 162011-90-7, Rofecoxib 169590-42-5, Celecoxib  
188627-80-7, Eftifibatide 191588-94-0, Tenecteplase

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(co-drug; preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands)

IT 50-48-6, Amitriptyline 72-69-5, Nortriptyline

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

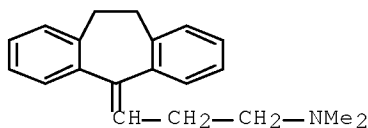
(co-drug; preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands)

RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-

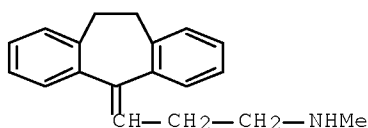
10/524815

dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 14 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:638859 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 143:153384

TITLE: Preparation of diaminothiadiazoles as CXCR- and CC-chemokine receptor ligands

INVENTOR(S): Biju, Purakkattil J.; Taveras, Arthur G.; Yu, Younong; Zheng, Junying; Chao, Jianhua; Aki, Cynthia J.; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacia Drug Discovery, Inc.

SOURCE: PCT Int. Appl., 593 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066147	A1	20050721	WO 2004-US42060	20041216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				

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AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2550189	A1	20050721	CA 2004-2550189	20041216
EP 1694659	A1	20060830	EP 2004-814266	20041216
EP 1694659	B1	20080827		

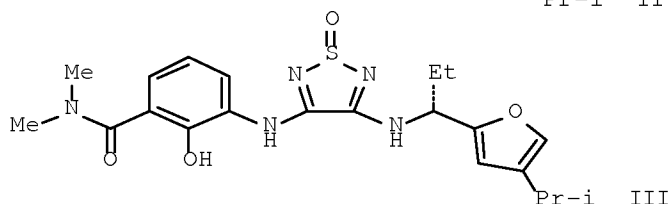
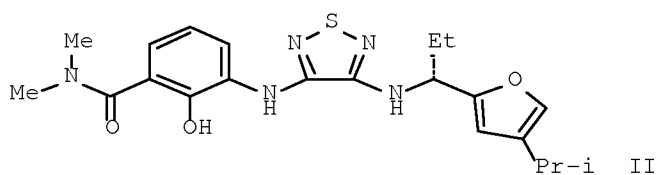
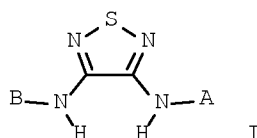
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

US 20060223864	A1	20061005	US 2004-13753	20041216
US 7338968	B2	20080304		
CN 1918138	A	20070221	CN 2004-80041695	20041216
JP 2007514746	T	20070607	JP 2006-545364	20041216
AT 406356	T	20080915	AT 2004-814266	20041216
ES 2308299	T3	20081201	ES 2004-814266	20041216
MX 2006007076	A	20060831	MX 2006-7076	20060619
HK 1087711	A1	20081128	HK 2006-109781	20060904
US 20080090823	A1	20080417	US 2007-861870	20070926

PRIORITY APPLN. INFO.:

US 2003-531311P	P	20031219
US 2003-531713P	P	20031222
US 2004-13753	A3	20041216
WO 2004-US42060	W	20041216

OTHER SOURCE(S): MARPAT 143:153384  
GI



AB Disclosed are diaminothiadiazoles I [A = (hetero)aryl, (hetero)arylmethyl (substituted at CH<sub>2</sub>), etc.; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and ischemia reperfusion injury, acute pain, acute and chronic inflammatory pain, and neuropathic pain using I. Although the methods of preparation are not claimed, hundreds of example preps. and/or

characterization data are included. For example, II was prepared in 43% yield from its monooxide III (preparation given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

- IC ICM C07D285-10
- ICS C07D417-12; C07D417-14; A61K031-433; A61K031-4436
- CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
- Section cross-reference(s): 1, 63
- IT AIDS (disease)
- Acne
- Alzheimer's disease
- Analgesics
- Anemia (disease)
- Angiogenesis
- Angiogenesis inhibitors
- Anti-AIDS agents
- Anti-Alzheimer's agents
- Anti-ischemic agents
- Antianginal agents
- Antiarthritics
- Antiasthmatics
- Antidiabetic agents
- Antimalarials
- Antiphospholipid syndrome
- Antirheumatic agents
- Antitumor agents
- Antitussives
- Antiulcer agents
- Antiviral agents
- Arthritis
- Asthma
- Atherosclerosis
- Behcet's syndrome
- Burn
- Celiac disease
- Central nervous system, neoplasm
- Cirrhosis
- Combination chemotherapy
- Common cold
- Cough
- Cystic fibrosis
- Dermatomyositis
- Diabetes mellitus
- Drug delivery systems
- Dyspnea
- Emphysema
- Encephalitis
- Fibrosis
- Gout
- Graves' disease
- Hepatitis virus
- Herpesviridae
- Human
- Human herpesvirus
- Human herpesvirus 8
- Hypercapnia
- Hypoxia
- Immunomodulators
- Lung, disease
- Lupus erythematosus
- Malaria

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Meningitis  
Multiple organ failure  
Multiple sclerosis  
Myasthenia gravis  
Myelodysplastic syndromes  
Myositis  
Neoplasm  
Osteoarthritis  
Osteoporosis  
Pruritus  
Psoriasis  
Respiratory system, disease  
Rheumatoid arthritis  
Sarcoidosis  
Sjogren syndrome  
Thrombosis  
Vitiligo

(preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands)

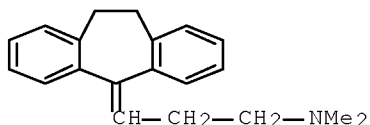
IT ~~50-48-6~~, Amitriptyline 53-86-1, Indomethacin ~~72-69-5~~  
, Nortriptyline 298-46-4, Carbamazepine 15687-27-1, Ibuprofen  
22071-15-4, Ketoprofen 22204-53-1, Naproxen 36322-90-4, Piroxicam  
60142-96-3, Gabapentin 84057-84-1, Lamotrigine 148553-50-8, Pregabalin  
162011-90-7, Rofecoxib 169590-42-5, Celecoxib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-drug; preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands)

IT ~~50-48-6~~, Amitriptyline ~~72-69-5~~, Nortriptyline  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-drug; preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands)

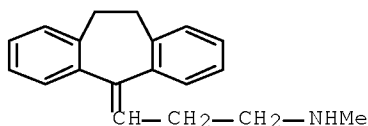
RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)





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OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)  
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 15 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:99226 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:197859

TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides,  
9H-carbazole-4-carboxamides, and  
dibenzo[b,d]thiophene-4-carboxamides as PDE4  
inhibitors for the treatment of inflammatory and  
allergic disorders

INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant A.;  
Lakdawala, Aftab D.; Karunakaran, Usha

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals, Inc. USA, USA

SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of Appl.  
No. PCT/IB04/000355.

CODEN: USXXCO

DOCUMENT TYPE: Patent

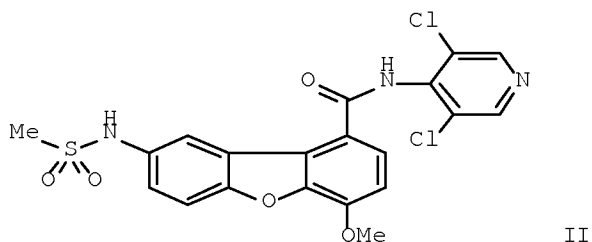
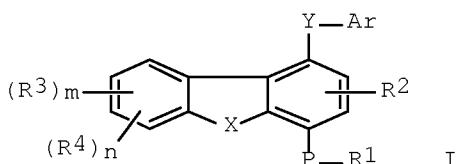
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050027129	A1	20050203	US 2004-821642	20040409
US 7223789	B2	20070529		
IN 2003MU00363	A	20050304	IN 2003-MU363	20030411
WO 2004089940	A1	20041021	WO 2004-IB355	20040211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ZA 2005008240	A	20060531	ZA 2005-8240	20051012
US 20070105854	A1	20070510	US 2006-536434	20060928
US 7384962	B2	20080610		
US 20070105855	A1	20070510	US 2006-536448	20060928
US 7393846	B2	20080701		
US 20090182143	A1	20090716	US 2008-131286	20080602
PRIORITY APPLN. INFO.:			IN 2003-MU363	A 20030411
			US 2003-519967P	P 20031113
			WO 2004-IB355	A2 20040211
			US 2004-821642	A3 20040409
			US 2006-536434	A1 20060928

OTHER SOURCE(S): MARPAT 142:197859  
GI



- AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6 (R5, R6 = H, alkyl, cycloalkyl, etc.), heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SOO-2, NRA; Y = CONR7, NR7SOO-2, SOO-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; Ra = H, alkyl, cycloalkyl, etc.; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1-carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).
- IC ICM C07D333-76  
ICS C07D209-82; C07D307-91
- INCL 549048000; 548444000; 549460000
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide  
prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic;  
tricyclic heterocycle prepn phosphodiesterase 4 inhibitor  
antiinflammatory antiallergic antidiabetic
- IT Inflammation  
(Crohn's disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease  
(Crohn's, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Eye, disease  
Inflammation  
(allergic conjunctivitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

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- IT Allergy  
Inflammation  
Nose, disease  
(allergic rhinitis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(allergic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis  
(atopic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease  
(cerebrovascular, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease  
Inflammation  
(chronic bronchitis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease  
(chronic obstructive pulmonary disease, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(chronic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(dementia, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(depression, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma  
(eosinophilic, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease  
(failure, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
(inflammation, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease  
Heart, disease  
Intestine, disease  
Joint, anatomical  
Lung, disease  
Skin, disease  
(inflammatory conditions or immune disorders, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

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- IT Intestine, disease
  - (inflammatory, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus
  - (insulin-resistant, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
  - Kidney, disease
    - (nephritis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors
- Alzheimer's disease
- Anti-Alzheimer's agents
- Anti-inflammatory agents
- Antiarthritics
- Antiasthmatics
- Antidepressants**
- Antidiabetic agents
- Antirheumatic agents
- Cardiovascular agents
- Drug delivery systems
- Human
- Immunomodulators
- Nervous system agents
  - (preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT **Tricyclic** compounds
  - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
    - (preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
- Gout
- Osteoarthritis
  - (rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
  - Spinal column, disease
    - (spondylitis, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
- Amnesia
- Asthma
- Central nervous system, disease
  - Cystic fibrosis**
- Immune disease
- Inflammation
- Multiple sclerosis
- Psoriasis
- Respiratory distress syndrome
- Rheumatoid arthritis
- Shock (circulatory collapse)

## Urticaria

(treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

## IT Inflammation

## Intestine, disease

(ulcerative colitis, rheumatoid, treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

## IT Eye, disease

## Inflammation

(uveitis; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-37-7P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
carboxamide 778576-41-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-54-8P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-methylpiperazin-4-  
yl]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-62-8P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-66-2P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[fur-2-  
yl]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-90-2P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-ethoxy-2-  
oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-  
oxoethylamino)dibenzo[b,d]furan-1-carboxamide

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(PDE4 inhibitor; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 778576-35-5P 778576-36-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-38-8P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[3-  
chloropropyl]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-40-2P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-  
butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium  
salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[fur-2-  
yl]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-45-7P,  
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778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

[bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
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 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[[trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(N-  
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 hydrochloride 778576-56-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-57-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(morpholin-4-  
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-60-6P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-61-7P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-65-1P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(1-  
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(hydroxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium  
 salt 778576-73-1P, N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
 carboxamide 778576-77-5P, N-(4-Methoxyphenyl)-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P,  
 N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-83-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
 carboxamide 778576-87-7P 778576-88-8P 778576-89-9P,  
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-hydroxy-2-  
 oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-  
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-  
 carboxamide 778576-95-7P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-  
 9H-carbazole-4-carboxamide 778576-96-8P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-  
 9H-carbazole-4-carboxamide 778576-97-9P,

N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-carbazole-4-carboxamide 778576-98-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt  
 778576-99-1P 778577-06-3P, N-(3,5-Dichloropyridin-4-yl)-4-  
 difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt  
 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(fur-2-  
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778581-69-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 2973-58-2P, 2-Bromoisovanillin 19688-46-1P,  
 3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P,  
 3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P,  
 2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P,  
 4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P,  
 4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P,  
 4-Cyclopentyloxy-3-hydroxybenzaldehyde 685873-89-6P,  
 2-Bromo-4-cyclopentyloxy-3-hydroxybenzaldehyde 685873-90-9P,  
 2-Bromo-4-cyclopentyloxy-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P,  
 4-Cyclopentyloxy-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P,  
 4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P,  
 4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P,  
 4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid  
 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P,  
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-  
 carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-  
 8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-  
 carboxamide 778576-29-7P, Methyl  
 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl  
 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl  
 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P,  
 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-  
 carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-  
 carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-  
 carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-  
 nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P,  
 N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-  
 carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P  
 778577-04-1P 778577-05-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 9036-21-9, Phosphodiesterase type 4

RL: BSU (Biological study, unclassified); BIOL (Biological study)

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(preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 836627-26-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9, 4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7, N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9, Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9, 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5, 2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isovanillin 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8, Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8, Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6, 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7, 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl 3-amino-4-methoxybenzoate 778576-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 16 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:1127375 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:74464

TITLE: Preparation of ~~tricyclic~~ compounds useful for the treatment of inflammatory and allergic disorders

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

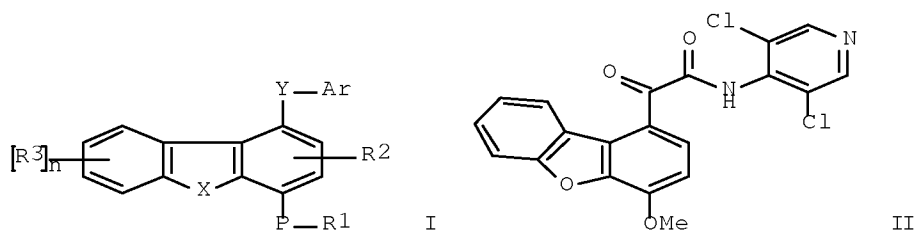
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2004111044	A1	20041223	WO 2004-IB1643	20040616
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			



10/524815

IN 2003MU00631 A 20050211 IN 2003-MU631 20030617  
 PRIORITY APPLN. INFO.: IN 2003-MU631 A 20030617  
 OTHER SOURCE(S): MARPAT 142:74464  
 GI



AB The title compds. I [R1-R3 = H, alkyl, cycloalkyl, aryl, etc.; n = 0-4; X = O, S(O)m, NRA (wherein m = 0-2; Ra = H, alkyl, cycloalkyl, etc.); P = O, S; Ar = (un)substituted aryl, arylalkyl, heterocyclyl, heteroaryl; Y = C(A)C(B)NR4 (wherein A, B = O, S, NRA; R4 = H, alkyl, OH, aryl, etc.)] which are novel phosphodiesterase type 4 (PDE4) inhibitors useful for the treatment of inflammatory and allergic disorders, were prepared Thus, reacting 2-(4-methoxydibenzo[b,f]furan-1-yl)-2-oxoacetic acid (preparation given) with 4-amino-3,5-dichloropyridine afforded II which showed IC50 of 184 nM against PDE4.

IC ICM C07D405-12  
 ICS A61K031-343

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
 Section cross-reference(s): 1

ST ~~tricyclic~~ compd prepn phosphodiesterase 4 PDE4 inhibitor  
 antiinflammatory; dibenzofuranyloxoacetamide prepn phosphodiesterase 4  
 PDE4 inhibitor antiinflammatory allergy asthma

IT Allergy inhibitors  
 Anti-Alzheimer's agents  
 Anti-inflammatory agents  
 Antiasthmatics  
 Antidepressants  
 Antidiabetic agents  
 Antirheumatic agents  
 Immunomodulators  
 (preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors for the  
 treatment of inflammatory and allergic disorders)

IT Allergy  
 Alzheimer's disease  
 Amnesia  
 Asthma  
 Central nervous system, disease  
 Cystic fibrosis  
 Eczema  
 Gout  
 Immune disease  
 Inflammation  
 Multiple sclerosis  
 Osteoarthritis  
 Psoriasis  
 Rheumatoid arthritis

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Shock (circulatory collapse)

Urticaria

(treating; preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors  
for

the treatment of inflammatory and allergic disorders)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 17 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:902155 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:384286

TITLE: Novel encochleation methods, cochleates and methods of  
use

INVENTOR(S): Mannino, Raphael J.; Gould-Fogerite, Susan;  
Krause-Elsmore, Sara L.; Delmarre, David; Lu, Ruying

PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA;  
University of Medicine and Dentistry of New Jersey

SOURCE: PCT Int. Appl., 195 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2004091578	A2	20041028	WO 2004-US11026	20040409
WO 2004091578	A3	20050331		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20050013854	A1	20050120	US 2004-822230	20040409
EP 1624858	A2	20060215	EP 2004-759375	20040409
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
US 20070237814	A1	20071011	US 2007-653434	20070111
US 20080009457	A1	20080110	US 2007-653093	20070111
PRIORITY APPLN. INFO.:			US 2003-461483P	P 20030409
			US 2003-463076P	P 20030415
			US 2003-499247P	P 20030828
			US 2003-502557P	P 20030911
			US 2003-532755P	P 20031224
			US 2004-537252P	P 20040115
			US 2004-556192P	P 20040324
			US 2004-822230	A1 20040409
			US 2004-822235	B1 20040409
			WO 2004-US11026	W 20040409

AB The invention generally relates to cochleate drug delivery vehicles. Disclose  
are novel methods for making cochleates and cochleate compns. that include  
introducing a cargo moiety to a liposome in the presence of a solvent. Also

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disclosed are cochleates and cochleate compns. that include an aggregation inhibitor, and optionally, a cargo moiety. Addnl., anhydrous cochleates that include a protonized cargo moiety, a divalent metal cation and a neg. charge lipid are disclosed. Methods of using the cochleate compns. of the invention, including methods of administration, are also disclosed.

IC ICM A61K009-127

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 2, 17, 18

IT Adenoma

Aggregation

Alopecia

Alzheimer's disease

Analgesics

Anesthetics

Animal virus

Anti-Alzheimer's agents

Anti-infective agents

Antiarthritics

Antiasthmatics

Antibacterial agents

Antibiotics

Anticholesteremic agents

Anticoagulants

Anticonvulsants

Antidepressants

Antidiabetic agents

Antihistamines

Antihypertensives

Antihypotensives

Antimicrobial agents

Antiobesity agents

Antioxidants

Antiparkinsonian agents

Antipsychotics

Antirheumatic agents

Antitumor agents

Antiviral agents

Arthritis

Asthma

Atherosclerosis

Autoimmune disease

Biliary tract, neoplasm

Blood coagulation disorders

Carcinoma

Carcinoma

Cations

Chelating agents

Cholinergic antagonists

Cognition enhancers

Cystic fibrosis

Cytoprotective agents

Cytotoxic agents

Dairy products

Decongestants

Detergents

Eczema

Esophagus, neoplasm

Expectorants

Flavoring materials

Fungicides

Gene therapy  
Genetic vectors  
Ginkgo  
Gout  
Graves' disease  
Gums and Mucilages  
Headache  
Hemophilia  
Hemostatics  
Hypercholesterolemia  
Hyperglycemia  
Hypericum  
Hypertension  
Hypolipemic agents  
Hypotension  
Imaging agents  
Immune disease  
Immunostimulants  
Immunosuppressants  
Infection  
Inflammation  
Leukemia  
Leukotriene antagonists  
Lung, neoplasm  
Lymphoma  
Malnutrition  
Mammary gland, neoplasm  
Melanoma  
Milk  
Mouthwashes  
Multiple sclerosis  
Muscular dystrophy  
Myasthenia gravis  
Mycosis  
Neoplasm  
Neuroglia, neoplasm  
Nutrients  
Obesity  
Organelle  
Osteoarthritis  
Ovary, neoplasm  
Packaging materials  
Pain  
Pancreas, neoplasm  
Parasitocides  
Parkinson's disease  
Pigments, biological  
Plasmids  
Prostate gland, neoplasm  
Psoriasis  
Psychotropics  
Rheumatoid arthritis  
Sarcoma  
Schizophrenia  
Skin, disease  
Stomach, neoplasm  
Sweetening agents  
Testis, neoplasm  
Tranquilizers  
Transplant rejection

Uterus, neoplasm

Vaccines

Vasoconstrictors

Vasodilators

Hyperlipidemia

RL: BIOL (Biological study)

(novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies  
 50-12-4, Mephenytoin 50-23-7, Hydrocortisone 50-24-8, Prednisolone  
~~50-48-6~~, Amitriptyline ~~50-49-7~~, Imipramine 51-61-6,  
 Dopamine, biological studies 52-53-9, Verapamil 53-06-5, Cortisone  
 53-86-1, Indomethacin 54-11-5, Nicotine 57-41-0, Phenytoin 57-92-1,  
 Streptomycin, biological studies 58-22-0, Testosterone 58-82-2,  
 Bradykinin 59-01-8, Kanamycin A 66-71-7, 1,10-Phenanthroline  
 67-20-9, Nitrofurantoin ~~72-69-5~~, Nortriptyline 77-41-8,  
 Methsuximide 77-67-8, Ethosuximide 79-09-4, Propionic acid, biological  
 studies 86-34-0, Phensuximide 86-35-1, Ethotoin 89-57-6, Mesalamine  
 103-90-2, Acetaminophen 110-91-8D, Morpholine, derivs. 112-38-9,  
 Undecylenic acid 113-15-5D, Ergotamine, derivs. ~~113-53-1~~,  
 Dothiepin 124-07-2, Caprylic acid, biological studies 125-33-7,  
 Primidone 126-07-8, Griseofulvin 127-48-0, Trimethadione 128-46-1,  
 Dihydrostreptomycin 130-26-7, Clioquinol 148-82-3, Melphalan  
 298-46-4, Carbamazepine 302-79-4, Vitamin A acid ~~303-49-1~~,  
 Clomipramine 379-68-0, 18-Hydroxydeoxycorticosterone 439-14-5,  
 Diazepam 458-37-7, Curcumin 512-64-1, Echinomycin 618-39-3,  
 Benzamidine 645-05-6, Hexamethylmelamine 777-11-7, Haloprogyn  
 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1403-66-3, Gentamycin  
 1404-04-2, Neomycin 1404-55-3, Ristocetin 1404-90-6, Vancomycin  
 1421-14-3, Propanidid ~~1668-19-5~~, Doxepin 1695-77-8,  
 Spectinomycin 2022-85-7, Flucytosine 2078-54-8, Propofol 2398-96-1,  
 Tolnaftate 2809-21-4 3947-65-7, Neamine 4696-76-8, Kanamycin B  
 7261-97-4, Dantrolene 7488-56-4, Selenium sulfide 7542-37-2,  
 Paromomycin 7681-93-8, Natamycin 8067-82-1, Alphadione 9002-60-2,  
 ACTH, biological studies 9004-10-8, Insulin, biological studies  
 9007-12-9, Calcitonin 9034-40-6, LH-RH 9041-90-1, Angiotensin I  
 9076-44-2, Chymostatin 11000-17-2, Vasopressin 11056-06-7, Bleomycin  
 11128-99-7, Angiotensin II 12687-51-3, Angiotensin III 13292-46-1,  
 Rifampin 14074-80-7, Zinc tetraphenyl porphyrin 15307-86-5, Diclofenac  
 15687-27-1, Ibuprofen 19794-93-5, Trazodone 21829-25-4, Nifedipine  
 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22832-87-7, Miconazole  
 nitrate 22916-47-8, Miconazole ~~23047-25-8~~, Lofepamine  
 23593-75-1, Clotrimazole 24305-27-9, Thyroid releasing hormone  
 25316-40-9, Adriamycin 25451-15-4, Felbamate 25546-65-0, Ribostamycin  
 27220-47-9, Econazole 28721-07-5, Oxcarbazepine 29767-20-2, Teniposide  
 30562-34-6, Geldanamycin 32986-56-4, Tobramycin 33069-62-4, Taxol  
 33507-63-0, Substance P (peptide) 36322-90-4, Piroxicam 36357-77-4,  
 Phosphoramidon 37321-09-8, Apramycin 37332-99-3, Avoparcin  
 37517-28-5, Amikacin 37691-11-5, Antipain 39319-82-9, Actinoidin  
 39324-30-6, Pepstatin 41621-49-2, Ciclopirox olamine 42924-53-8,  
 Nabumetone 51050-59-0, 3,4-Dichloroisocoumarin 51110-01-1,  
 Somatostatin 51798-45-9, Elastatinal 53123-88-9, Rapamycin  
 54651-05-7, Echinocandin B 54910-89-3, Fluoxetine 55123-66-5,  
 Leupeptin 56391-56-1, Netilmicin 58391-28-9, Leucokinin 58814-86-1,  
 Aculeacin A 58970-76-6, Bestatin 59277-89-3, Acyclovir 59729-33-8,  
 Citalopram 59865-13-3, Cyclosporin 60617-12-1,  $\beta$ -Endorphin  
 61036-62-2, Teicoplanin 61318-90-9, Sulconazole 61869-08-7, Paroxetine  
 64211-45-6, Oxiconazole 64872-76-0, Butoconazole 65277-42-1,  
 Ketoconazole 65472-88-0, Naftifine 67655-94-1, Amastatin 67915-31-5,

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Terconazole 68291-97-4, Zonisamide 70288-86-7, Ivermectin  
 71125-38-7, Meloxicam 71620-89-8, Reboxetine 74913-18-1, Dynorphin  
 78628-80-5, Terbinafine hydrochloride 79404-91-4, Cilofungin  
 79617-96-2, Sertraline 80619-41-6, Echinocandin 84057-84-1,  
 Lamotrigine 84625-61-6, Itraconazole 85650-52-8, Mirtazapine  
 86386-73-4, Fluconazole 93390-81-9, Fosphenytoin 93413-69-5,  
 Venlafaxine 97240-79-4, Topiramate 101828-21-1, Butenafine  
 102767-28-2, Levetiracetam 105462-24-6 110588-57-3, Saperconazole  
 114977-28-5, Taxotere 118850-71-8 118850-72-9 118850-73-0  
 127779-20-8, Saquinavir 135882-23-4, Pneumocandin A4 137234-62-9,  
 Voriconazole 150378-17-9, Indinavir 155213-67-5, Ritonavir  
 159445-62-2, Orientiparcin 159989-64-7, Nelfinavir 161814-49-9,  
 Amprenavir 162011-90-7, Rofecoxib 162808-62-0, Caspofungin  
 166663-25-8, Anidulafungin 235114-32-6, Micafungin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(novel encochleation methods and cochleates and methods of use for  
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 inhibitors)

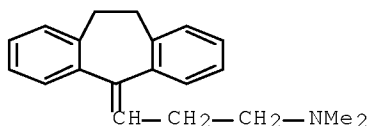
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 303-49-1, Clomipramine 1668-19-5, Doxepin  
 23047-25-8, Lofepramine 85650-52-8, Mirtazapine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(novel encochleation methods and cochleates and methods of use for  
 delivery of drugs and other agents using liposomes and aggregation  
 inhibitors)

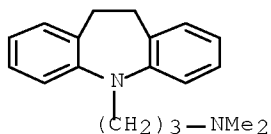
RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-  
 dimethyl- (CA INDEX NAME)



RN 50-49-7 ZCAPLUS

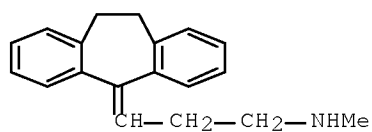
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA  
 INDEX NAME)



RN 72-69-5 ZCAPLUS

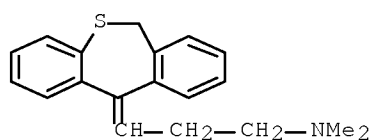
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-  
 methyl- (CA INDEX NAME)

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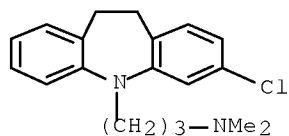
RN 113-53-1 ZCAPLUS

CN 1-Propanamine, 3-dibenzo[b,e]thiepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



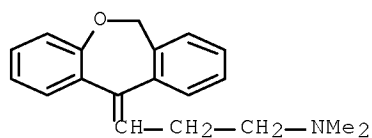
RN 303-49-1 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 1668-19-5 ZCAPLUS

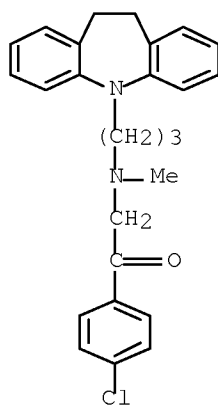
CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



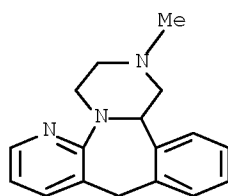
RN 23047-25-8 ZCAPLUS

CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]methylamino]- (CA INDEX NAME)

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RN	85650-52-8	ZCAPLUS
CN	Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)	



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

L91 ANSWER 18 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2004:878393 ZCAPLUS Full-text  
DOCUMENT NUMBER: 141:366121  
TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides,  
9H-carbazole-4-carboxamides, and  
dibenzo[b,d]thiophene-4-carboxamides as PDE4  
inhibitors for the treatment of inflammatory and  
allergic disorders  
INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant Atmaram;  
Lakdawala, Aftab Dawoodbhai; Karaunakaran, Usha  
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India  
SOURCE: PCT Int. Appl., 121 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004089940	A1	20041021	WO 2004-IB355	20040211
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,			



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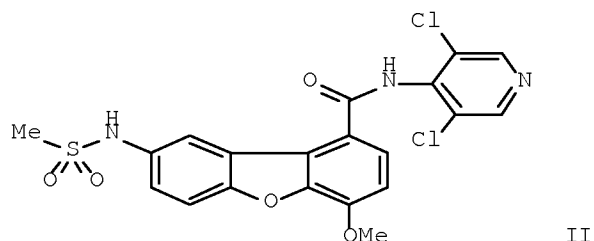
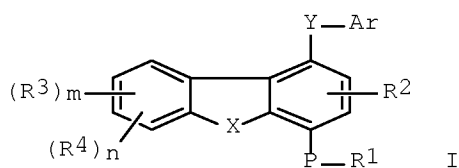
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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW,  
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,  
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 2003MU00363	A	20050304	IN 2003-MU363	20030411
AU 2004228453	A1	20041021	AU 2004-228453	20040211
CA 2522023	A1	20041021	CA 2004-2522023	20040211
EP 1620429	A1	20060201	EP 2004-710093	20040211
EP 1620429	B1	20090401		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004009747	A	20060509	BR 2004-9747	20040211
CN 1829711	A	20060906	CN 2004-80016048	20040211
JP 2006522789	T	20061005	JP 2006-506259	20040211
NZ 542882	A	20071026	NZ 2004-542882	20040211
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AP 2008	A	20090630	AP 2005-3424	20040211
US 20050027129	A1	20050203	US 2004-821642	20040409
US 7223789	B2	20070529		
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NO 2005005316	A	20060111	NO 2005-5316	20051110
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US 7393846	B2	20080701		
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PRIORITY APPLN. INFO.:

IN 2003-MU363	A	20030411
US 2003-519967P	P	20031113
WO 2004-IB355	W	20040211
US 2004-821642	A3	20040409
US 2006-536434	A1	20060928

OTHER SOURCE(S): CASREACT 141:366121; MARPAT 141:366121  
GI



- AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6, heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SO0-2, NRA; Y = CONR7, NR7SO0-2, SO0-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1-carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).
- IC ICM C07D405-12  
ICS C07D405-14; C07D307-91; C07D401-12; C07D409-12; A61K031-4427; A61P029-00
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide  
prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic;  
tricyclic heterocycle prepn phosphodiesterase 4 inhibitor  
antiinflammatory antiallergic antidiabetic
- IT Inflammation  
(Crohn's disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease  
(Crohn's, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Eye, disease  
Inflammation  
(allergic conjunctivitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Eye, disease  
Inflammation  
(allergic conjunctivitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Inflammation  
Nose, disease  
(allergic rhinitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(allergic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis  
(atopic, rheumatoid, treatment of; preparation of tricyclic

- heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease  
(cerebrovascular, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease  
Inflammation  
(chronic bronchitis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease  
(chronic obstructive pulmonary disease, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(chronic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Anti-inflammatory agents  
(chronic; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(dementia, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(depression, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma  
(eosinophilic, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease  
(failure, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
(inflammation, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease  
Heart, disease  
Intestine, disease  
Joint, anatomical  
Lung, disease  
Skin, disease  
(inflammatory conditions or immune disorders, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease  
(inflammatory, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus  
(insulin-resistant, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

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- IT Inflammation
  - Kidney, disease
    - (nephritis, treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors
  - Anti-Alzheimer's agents
  - Anti-inflammatory agents
  - Antiarthritics
  - Antiasthmatics
  - ~~Antidepressants~~
  - Antidiabetic agents
  - Antirheumatic agents
  - Cardiovascular agents
  - Drug delivery systems
  - Human
  - Immunomodulators
  - Nervous system agents
  - Polymorphism (crystal)
    - (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tumor necrosis factors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT ~~Tricyclic~~ compounds
  - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
    - (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
- Gout
- Osteoarthritis
  - (rheumatoid, treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
  - Spinal column, disease
    - (spondylitis, rheumatoid, treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
- Amnesia
- Asthma
- Central nervous system, disease
- ~~Cystic~~ fibrosis
- Immune disease
- Inflammation
- Multiple sclerosis
- Psoriasis
- Respiratory distress syndrome
- Rheumatoid arthritis
- Shock (circulatory collapse)
- Urticaria
  - (treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and

insulin resistant diabetes)

IT Inflammation  
Intestine, disease  
(ulcerative colitis, rheumatoid, treatment of; preparation of  
~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of  
immune and inflammatory disorders and insulin resistant diabetes)

IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-37-7P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
carboxamide 778576-41-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-54-8P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (N-methylpiperazin-4-  
yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-62-8P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-66-2P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (fur-2-  
yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-90-2P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-ethoxy-2-  
oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-  
oxoethylamino)dibenzo[b,d]furan-1-carboxamide  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); RACT (Reactant or reagent); USES (Uses)  
(PDE4 inhibitor; preparation of ~~tricyclic~~ heterocycles as PDE4  
inhibitors for treatment of immune and inflammatory disorders and  
insulin resistant diabetes)

IT 778576-35-5P 778576-36-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-38-8P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (3-  
chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-40-2P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-  
butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium  
salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (fur-2-  
yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-45-7P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-48-0P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[[ (isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

[[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(N-methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 hydrochloride 778576-56-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-57-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(morpholin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-60-6P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-61-7P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-65-1P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[[(1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium  
 salt 778576-73-1P, N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
 carboxamide 778576-77-5P, N-(4-Methoxyphenyl)-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P,  
 N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-83-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
 carboxamide 778576-87-7P 778576-88-8P 778576-89-9P,  
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-hydroxy-2-  
 oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-  
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-  
 carboxamide 778576-95-7P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-  
 methyl-6-[(methylsulfonyl)amino]-9H-carbazole-4-carboxamide  
 778576-96-8P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-  
 [(ethylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-97-9P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-  
 carbazole-4-carboxamide 778576-98-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt  
 778576-99-1P 778577-06-3P, N-(3,5-Dichloropyridin-4-yl)-4-  
 difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt  
 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[[(fur-2-  
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778581-69-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 2973-58-2P, 2-Bromoisovanillin 19688-46-1P,  
 3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P,  
 3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P,  
 2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P,  
 4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P,  
 4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P,  
 4-Cyclopentyloxy-3-hydroxybenzaldehyde 685873-89-6P,  
 2-Bromo-4-cyclopentyloxy-3-hydroxybenzaldehyde 685873-90-9P,  
 2-Bromo-4-cyclopentyloxy-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P,  
 4-Cyclopentyloxy-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P,  
 4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P,  
 4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P,  
 4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid  
 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P,  
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-carboxamide 778576-29-7P, Methyl  
 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl  
 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl  
 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P,  
 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P,  
 N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P  
 778577-04-1P 778577-05-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 9036-21-9, Phosphodiesterase type 4 9040-59-9, Phosphodiesterase 1  
 9068-52-4, Phosphodiesterase type 5

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9,  
 4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7,  
 N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9,  
 Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9,  
 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5,

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2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isovanillin 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8, Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8, Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6, 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7, 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl 3-amino-4-methoxybenzoate 778576-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 19 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:675744 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:207059

TITLE: Tricyclic compounds (dibenzofurans, dibenzothiophenes, carbazoles, and analogs) with PDE4 inhibitory activity, useful for the treatment of inflammatory and allergic disorders, process for their preparation, and methods of use

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Bedekar, Sarika Suhas

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

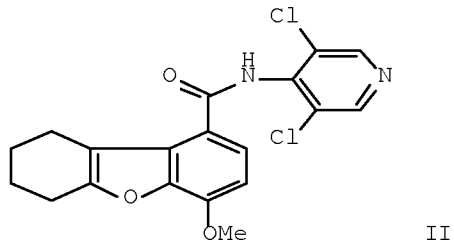
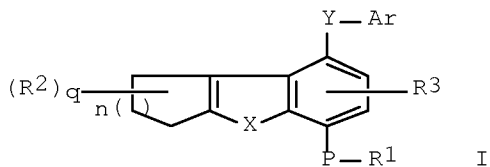
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004069831	A1	20040819	WO 2004-IB330	20040210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00177	A	20050204	IN 2003-MU177	20030210
PRIORITY APPLN. INFO.:			IN 2003-MU177	A 20030210
OTHER SOURCE(S):	MARPAT	141:207059		
GI				





- AB The invention relates to novel heterocyclic compds. and their analogs, tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, appropriate oxides, and pharmaceutically acceptable solvates, as well as pharmaceutical compns. containing them. The invention more particularly relates to novel phosphodiesterase type 4 (PDE4) inhibitors. In particular, compds. I and their aforementioned related compds. are claimed [wherein: R1, R2, R3 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, protecting groups, or two ortho R2 may form 3- to 7-membered ring with 0-2 optional NR1/O/S heteroatoms; X = O, S(O)m, NH, or NR5; Y = CONR4, NR4SO2, SO2NR4, and NR4CO; P = O or S; q = 0-5; n = 1-3; m = 0-2; Ar = (un)substituted aryl, arylalkyl, heterocyclic, or heteroaryl; R4 = H, (un)substituted alkyl, OH, OR1, aryl, or heterocyclic; R5 = (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, and protecting groups]. The compds. (33 examples) were prepared and tested for PDE4 inhibitory activity. For instance, 6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-carboxylic acid chloride [prepared in 5 steps from 2-methoxyphenol (guaicol) and 2-bromocyclohexanone] was amidated with 4-amino-3,5-dichloropyridine in DMF/THF to give invention compound II. This compound had an IC50 value of 0.4468 nM against PDE4 in vitro.
- IC ICM C07D405-12  
ICS C07D409-12; C07D401-12; C07D307-92; A61K031-343; A61K031-381; A61K031-403
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1
- ST ~~tricyclic~~ prepn phosphodiesterase 4 inhibitor antiinflammatory  
antiallergic; pyridyl dibenzofuran dibenzothiophene carbazole PDE4  
inhibitor inflammation allergy treatment
- IT Allergy inhibitors  
Anti-Alzheimer's agents  
Anti-inflammatory agents  
Antiarthritics  
Antiasthmatics  
Antidepressants  
Antidiabetic agents  
Cardiovascular agents

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Cognition enhancers

Immunomodulators

Immunosuppressants

Nervous system agents

(preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

IT Alzheimer's disease

Amnesia

Asthma

Central nervous system, disease

**Cystic fibrosis**

Eczema

Gout

Immune disease

Inflammation

Multiple sclerosis

Osteoarthritis

Psoriasis

Respiratory distress syndrome

Rheumatoid arthritis

Shock (circulatory collapse)

Urticaria

(treatment of; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 20 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:370918 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:391192

TITLE: Preparation of dibenzofuran/dibenzothiophene derivatives useful for the treatment of inflammatory and allergic disorders

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 254 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

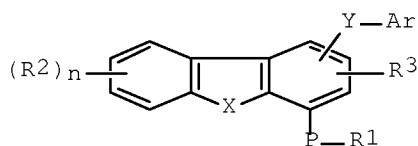
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

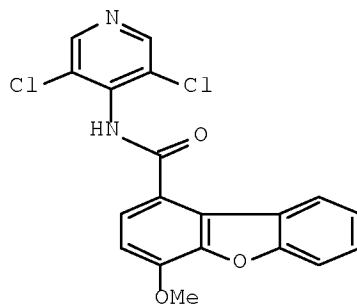
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004037805	A1	20040506	WO 2003-IB4442	20031008
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

10/524815

IN 2002MU00922	A	20050304	IN 2002-MU922	20021023
CA 2503015	A1	20040506	CA 2003-2503015	20031008
AU 2003269317	A1	20040513	AU 2003-269317	20031008
EP 1554262	A1	20050720	EP 2003-751096	20031008
EP 1554262	B1	20071205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014721	A	20050802	BR 2003-14721	20031008
CN 1729181	A	20060201	CN 2003-80107246	20031008
JP 2006506379	T	20060223	JP 2004-546246	20031008
AT 380185	T	20071215	AT 2003-751096	20031008
ES 2298552	T3	20080516	ES 2003-751096	20031008
ZA 2005002969	A	20060222	ZA 2005-2969	20050413
US 20060178418	A1	20060810	US 2005-532273	20050926
US 7238725	B2	20070703		
US 20080146810	A1	20080619	US 2007-769074	20070627
PRIORITY APPLN. INFO.:			IN 2002-MU922	A 20021023
			WO 2003-IB4442	W 20031008
			US 2005-532273	A1 20050926
OTHER SOURCE(S):		MARPAT 140:391192		
GI				



I



II

AB Title compds. I [R1-3 = H, alk(en/yn)yl, cycloalkyl, etc.; P = O, S; n = 0-4; Ar = (un)substituted aryl, etc.; Y = carboxamido, aminosulfonyl, etc.] are prepared For instance, 4-methoxydibenzofuran-1-carboxylic acid (preparation given) is converted to the corresponding acid chloride (PhH, SOCl<sub>2</sub>, reflux, 4 h) and treated with 4-amino-3,5-dichloropyridine (DMF/THF, NaH, -10°) to give II. II has IC<sub>50</sub> = 0.8 nM for PDE4. I are useful for the treatment of inflammatory conditions, diseases of the central nervous and insulin resistant diabetes.

IC ICM C07D307-91  
ICS C07D333-76; C07D209-88; C07D405-12; C07D401-12; C07D409-12; C07D405-14; A61K031-403; A61K031-34; A61K031-381; A61P037-00; A61P025-00; A61P003-10

CC 27-9 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1, 63

ST tricyclic dibenzofuran dibenzothiophene inflammatory allergic process  
prepn

IT Alzheimer's disease  
Amnesia  
Anti-inflammatory agents

10/524815

Antiarthritics  
Antiasthmatics  
Antidepressants  
Antidiabetic agents  
Antirheumatic agents  
Asthma  
Cystic fibrosis  
Diabetes insipidus  
Diabetes mellitus  
Gout  
Human  
Immune disease  
Inflammation  
Multiple sclerosis  
Nervous system agents  
Osteoarthritis  
Psoriasis  
Respiratory distress syndrome  
Rheumatoid arthritis

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)  
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 21 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:935594 ZCAPLUS Full-text

DOCUMENT NUMBER: 136:69730

TITLE: Preparation of  
1,3-bis-(substituted-phenyl)-2-propen-1-ones as VCAM-1  
inhibitors for treatment of inflammatory disorders  
INVENTOR(S): Meng, Charles Q.; Ni, Liming; Sikorski, James A.;  
Hoong, Lee K.

PATENT ASSIGNEE(S): Atherogenics, Inc., USA

SOURCE: PCT Int. Appl., 220 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098291	A2	20011227	WO 2001-US19720	20010620
WO 2001098291	A3	20020516		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
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CA 2413878	A1	20011227	CA 2001-2413878	20010620
BR 2001011889	A	20030624	BR 2001-11889	20010620
EP 1330448	A2	20030730	EP 2001-946583	20010620
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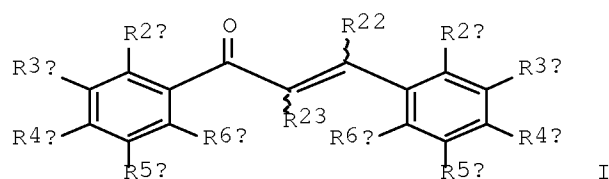
10/524815

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JP 2004501147	T	20040115	JP 2002-504247	20010620
NZ 523443	A	20041126	NZ 2001-523443	20010620
MX 2002012660	A	20040514	MX 2002-12660	20021218
IN 2003DN00008	A	20060609	IN 2003-DN8	20030101
ZA 2003000134	A	20051006	ZA 2003-134	20030106
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US 7078431	B2	20060718		
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US 20060258735	A1	20061116	US 2006-485940	20060713

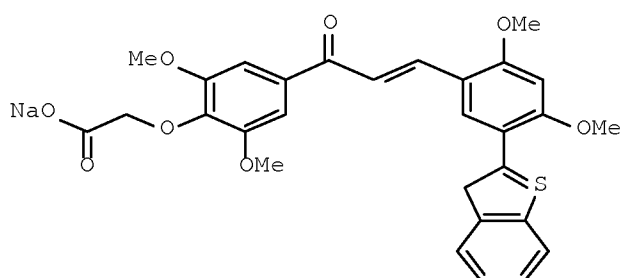
PRIORITY APPLN. INFO.:

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US 2000-255934P	P	20001215
US 2001-886348	A1	20010620
WO 2001-US19720	W	20010620
US 2003-443470	A1	20030521

OTHER SOURCE(S): MARPAT 136:69730  
GI



I



II

AB Title compds. I [wherein R2a, R3a, R4a, R5a, R6a, R2b, R3b, R4b, R5b, and R6b = independently H, (cyclo)alkyl, (hetero)aryl, carbocyclyl, (halo)alkylthio, (un)substituted alkoxy or amino, (halo)acyl, amido, (halo)alkylsulfonyl, aminocarbonyl, alkenyl, alkynyl, halo, OH, SH, CN, NO2, SO3H, sulf(on)amido, PO3H2, alditol, carbohydrate, amino acid, etc.; R22 and R23 = independently H or alkyl; or R22 and R6a or R23 and R6a can join together to form a bridged carbocycle, (hetero)aryl, or heterocycle; R2a and R3a, R3a and R4a, R4a and R5a, R5a and R6a, R2b and R3b, R3b and R4b, R4b and R5b, or R5b and R6b and independently join to form a bridged (un)substituted carbocycle, cycloalkenyl, cycloalk(en)ylcarbonyl, (hetero)aryl, heterocycle, or alkylenedioxy; and the E or Z isomers thereof] were prepared to inhibit the expression of VCAM-1. For example, 3',5'-dimethoxy-4'-hydroxyacetophenone was treated with Et glycolate, PPh3, and di-Et azodicarboxylate in THF to give 4'-ethoxycarbonylmethoxy-3',5'-dimethoxyacetophenone (90%). Coupling the acetophenone and 5-(benzo[b]thien-2-yl)-2,4-dimethoxybenzaldehyde (preparation given) in the presence of NaOH in absolute EtOH afforded the 1,3-diphenyl-2-propen-1-one II (39%), which stimulated cultured human aortic smooth muscle cell activity with

IC50 of 0.45  $\mu$ M. I are useful for the treatment of inflammatory disorders that are mediated by VCAM-1, including arthritis, asthma, dermatitis, cystic fibrosis, post transplantation late and chronic solid organ rejection, multiple sclerosis, systemic lupus erythematosus, inflammatory bowel diseases, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, post-angioplasty restenosis, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves disease, gastrointestinal allergies, conjunctivitis, atherosclerosis, coronary artery disease, angina and small artery disease.

IC ICM C07D333-00

CC 27-8 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT Cystic fibrosis

Dermatitis

Graves' disease

Psoriasis

Transplant rejection

(treatment; preparation of bis(substituted phenyl)propenones as VCAM-1 inhibitors for treatment of inflammatory disorders)

IT Antidepressants

(tricyclic; co-administration of bis(substituted phenyl)propenone VCAM-1 inhibitors with other biol. agents)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 22 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:338762 ZCAPLUS Full-text

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

INVENTOR(S): Farr, Spencer

PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA

SOURCE: PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105

US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a

subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IC ICM C12Q001-68

ICS G01N033-50

CC 3-4 (Biochemical Genetics)

Section cross-reference(s): 1, 6, 7, 13, 15

IT CFTR (cystic fibrosis transmembrane conductance regulator)

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(methods of determining individual hypersensitivity to a pharmaceutical

agent

from gene expression profile)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies  
 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8,  
 Prednisolone 50-28-2, Estradiol, biological studies 50-44-2,  
 6-Thiopurine ~~50-48-6~~, Amitriptyline 50-55-5, Reserpine  
 50-76-0, Actinomycin D 50-78-2, Aspirin 51-06-9, Procainamide  
 51-21-8, Fluorouracil 51-34-3, Scopolamine 51-48-9, Levothyroxine,  
 biological studies 51-49-0, Dextrothyroxine 51-55-8, Atropine,  
 biological studies 51-75-2, Mechlorethamine 52-01-7, Spironolactone  
 52-53-9, Verapamil 52-67-5, Penicillamine 52-86-8, Haloperidol  
 53-03-2, Prednisone 53-06-5, Cortisone 53-19-0, Mitotane 53-33-8,  
 Paramethasone 53-86-1, Indomethacin 54-05-7, Chloroquine 54-11-5,  
 Nicotine 54-31-9, Furosemide 54-36-4, Metyrapone 54-85-3, Isoniazid  
 55-63-0, Nitroglycerin 55-65-2, Guanethidine 55-98-1, Busulfan  
 56-54-2, Quinidine 56-75-7, Chloramphenicol 57-22-7, Vincristine  
 57-41-0, Phenytoin 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol  
 57-66-9, Probenecid 57-83-0, Progesterin, biological studies 57-96-5,  
 Sulfapyrazole 58-05-9, Leucovorin 58-14-0, Pyrimethamine 58-32-2,  
 Dipyridamole 58-39-9, Perphenazine 58-54-8, Ethacrynic acid 58-55-9,  
 Theophylline, biological studies 58-61-7, Adenosine, biological studies  
 58-74-2, Papaverine 58-93-5, Hydrochlorothiazide 58-94-6, Thiazide  
 59-05-2, Methotrexate 59-42-7, Phenylephrine 59-43-8, Thiamine,  
 biological studies 59-92-7, Levodopa, biological studies 59-99-4,  
 Neostigmine 60-40-2, Mecamylamine 60-54-8, Tetracycline 60-79-7,  
 Ergonovine 60-87-7, Promethazine 61-32-5, Methicillin 61-72-3,  
 Cloxacillin 64-75-5, Tetracycline hydrochloride 64-77-7, Tolbutamide  
 64-86-8, Colchicine 65-23-6, Pyridoxine 66-79-5, Oxacillin 66-97-7,  
 Psoralen 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-68-5,  
 Dimethyl sulfoxide, biological studies 68-22-4D, Norethindrone, mixture  
 with ethinyl estradiol 68-41-7, Cycloserine 68-88-2, Hydroxyzine  
 69-53-4, Ampicillin 69-72-7, biological studies 69-89-6, Xanthine  
 73-24-5, 6-Aminopurine, biological studies 73-31-4, Melatonin 76-42-6,  
 Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0,  
 Dicyclomine 77-36-1, Chlorthalidone 78-44-4, Carisoprodol 80-08-0,  
 Dapsone 81-23-2, Dehydrocholic acid 81-81-2, Warfarin 82-92-8,  
 Cyclizine 82-95-1, Buclizine 83-43-2, Methylprednisolone 83-73-8,

Iodoquinol 83-89-6, Quinacrine 83-98-7, Orphenadrine 86-54-4, Hydralazine 89-57-6, Mesalamine 90-34-6, Primaquine 90-82-4, Pseudoephedrine 91-64-5, Coumarin 92-13-7, Pilocarpine 92-84-2, Phenothiazine 93-14-1, Guaifenesin 94-20-2, Chlorpropamide 94-36-0, Benzoyl peroxide, biological studies 94-78-0, Phenazopyridine 95-25-0, Chlorzoxazone 96-64-0, Soman 97-77-8, Disulfiram 99-66-1, Valproic acid 100-33-4, Pentamidine 100-97-0, Methenamine, biological studies 101-31-5, Hyoscyamine 103-90-2, Acetaminophen 113-18-8, Ethchlorvynol 113-42-8, Methylergonovine 113-45-1, Methylphenidate 114-07-8, Erythromycin 114-86-3, Phenformin 118-42-3, Hydroxychloroquine 122-09-8, Phentermine 123-56-8, Succinimide 123-63-7, Paraldehyde 124-94-7, Triamcinolone 125-29-1, Hydrocodone 125-33-7, Primidone 125-64-4, Methypylon 125-71-3, Dextromethorphan 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 126-52-3, Ethinamate 127-07-1, Hydroxyurea 127-69-5, Sulfisoxazole 128-13-2, Ursodiol 130-95-0, Quinine 132-17-2, Benztropine 133-10-8, Sodium p-aminosalicylate 137-58-6, Lidocaine 138-56-7, Trimethobenzamide 144-11-6, Trihexyphenidyl 147-52-4, Nafcillin 147-94-4, AraC 148-82-3, Melphalan 154-21-2, Lincomycin 154-42-7, Thioguanine 154-93-8, Carmustine 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-50-0, Propantheline 299-42-3, Ephedrine 300-62-9D, Amphetamine, mixed 300-62-9D, Amphetamine, mixed salts 302-17-0, Chloral hydrate 302-79-4, Tretinoin 303-53-7, Cyclobenzaprine 305-03-3, Chlorambucil 315-30-0, Allopurinol 321-64-2, Tacrine 346-18-9, Polythiazide 361-37-5, Methysergide 363-24-6, Dinoprostone 364-62-5, Metoclopramide 378-44-9, Betamethasone 389-08-2, Nalidixic acid 395-28-8, Isoxsuprine 439-14-5, Diazepam 443-48-1, Metronidazole 446-86-6, Azathioprine 456-59-7, Cyclophosphamide 461-72-3, Hydantoin 463-04-7, Amyl nitrite 469-62-5, Propoxyphene 474-25-9, Chenodiol 480-30-8, Dichloralphenazone 484-23-1, Dihydralazine 503-01-5, Isometheptene 512-15-2, Cyclopentolate 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 526-36-3, Xylometazoline 536-33-4, Ethionamide 541-15-1, Levocarnitine 546-88-3, Acetohydroxamic acid 555-30-6, Methyl dopa 564-25-0, Doxycycline 569-65-3, Meclizine 577-11-7, Docusate sodium 596-51-0, Glycopyrrolate 599-79-1, Sulfasalazine 603-50-9, Bisacodyl 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin 671-16-9, Procarbazine 672-87-7, Metyrosine 674-38-4, Bethanechol 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 745-65-3, Alprostadil 791-35-5, Chlophedianol 797-63-7, Levonorgestrel 797-64-8D, L-Norgestrel, ethinyl estradiol mixture 846-49-1, Lorazepam 846-50-4, Temazepam 911-45-5, Clomiphene 915-30-0, Diphenoxylate 962-58-3, Diazoxon 968-93-4, Testolactone 972-02-1, Diphenidol 990-73-8, Fentanyl citrate 1134-47-0, Baclofen 1143-38-0, Anthralin 1321-13-7, Potassium aminobenzoate 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1404-04-2, Neomycin 1404-04-2D, Neomycin, mixture with polymyx/HC 1404-90-6, Vancomycin 1406-05-9, Penicillin 1491-59-4, Oxymetazoline 1622-61-3, Clonazepam 1953-02-2, Tiopronin 1977-10-2, Loxapine 2152-34-3, Pemoline 2152-44-5, Betamethasone valerate 2447-57-6, Sulfadoxine 2451-01-6, Terpin hydrate 2609-46-3, Amiloride 2809-21-4 2998-57-4, Estramustine 3116-76-5, Dicloxacillin 3313-26-6, Thiothixene 3385-03-3, Flunisolide 3485-14-1, Cyclacillin 3737-09-5, Disopyramide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(methods of determining individual hypersensitivity to a pharmaceutical

agent

from gene expression profile)

IT 3778-73-2, Iphosphamide 3930-20-9, Sotalol 4205-90-7, Clonidine 4419-39-0, Beclomethasone 4499-40-5, Oxtriphylline, biological studies



4618-18-2, Lactulose 4697-36-3, Carbenicillin 4759-48-2, Isotretinoin  
 5051-62-7, Guanabenz 5543-57-7, (s)-Warfarin 5633-20-5, Oxybutynin  
 5786-21-0, Clozapine 6190-39-2, Dihydroergotamine mesylate 6493-05-6,  
 Pentoxifylline 6621-47-2, Perhexiline 7020-55-5, Clidinium  
 7235-40-7, Beta carotene 7261-97-4, Dantrolene 7416-34-4, Molindone  
 7439-93-2, Lithium, biological studies 7447-40-7, Potassium chloride,  
 biological studies 7481-89-2, Zalcitabine 7487-88-9, Magnesium  
 sulfate, biological studies 7648-98-8, Ambenonium 7681-11-0, Potassium  
 iodide, biological studies 7681-93-8, Natamycin 7683-59-2,  
 Isoproterenol 8029-99-0, Paregoric 8049-47-6, Pancreatin 8050-81-5,  
 Simethicone 8063-07-8, Kanamycin 8067-24-1, Ergoloid mesylates  
 9001-27-8, BLOOD-coagulation factor VIII 9001-75-6, Pepsin 9004-10-8,  
 Insulin, biological studies 9004-67-5, Methyl cellulose 9005-49-6,  
 Enoxaparin, biological studies 9007-92-5, Glucagon, biological studies  
 9039-53-6, Urokinase 9046-56-4, Ancrod 10118-90-8, Minocycline  
 10238-21-8, Glyburide ~~10262-69-8~~, Maprotiline 10540-29-1,  
 Tamoxifen 11041-12-6, Cholestyramine 11056-06-7, Bleomycin  
 11111-12-9, Cephalosporin 12174-11-7, Attapulgit 12244-57-4, Gold  
 sodium thiomalate 12650-69-0, Mupirocin 12794-10-4D, Benzodiazepine,  
 derivs. 13010-47-4, Lomustine 13292-46-1, Rifampin 13311-84-7,  
 Flutamide 13392-28-4, Rimantadine 13647-35-3, Trilostane  
~~14028-44-5~~, Amoxapine 14124-50-6 14611-51-9, Selegiline  
 14769-73-4, Levamisole 14838-15-4, Phenylpropanolamine 14882-18-9,  
 Bismuth subsalicylate 15301-69-6, Flavoxate 15307-86-5, Diclofenac  
 15663-27-1, Cisplatin 15686-71-2, Cephalixin 15687-27-1, Ibuprofen  
 15722-48-2, Olsalazine 16051-77-7, Isosorbide mononitrate 16068-46-5,  
 Potassium phosphate 16110-51-3, Cromolyn 16590-41-3, Naltrexone  
 16679-58-6, Desmopressin 17230-88-5, Danazol 17784-12-2, Sulfacytine  
 18323-44-9, Clindamycin 18559-94-9, Albuterol 18883-66-4, Streptozocin  
 19216-56-9, Prazosin 19794-93-5, Trazodone 20537-88-6, Amifostine  
 20830-75-5, Digoxin 20830-81-3, Daunomycin 21256-18-8, Oxaprozin  
 21829-25-4, Nifedipine 22204-53-1, Naproxen 22232-71-9, Mazindol  
 23031-32-5, Terbutaline sulfate 23214-92-8, Doxorubicin 23288-49-5,  
 Probucol 25322-68-3, Polyethylene glycol 25451-15-4, Felbamate  
 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 26652-09-5,  
 Ritodrine 26787-78-0, Amoxicillin 26807-65-8, Indapamide 26839-75-8,  
 Timolol 27203-92-5, Tramadol 27262-47-1, Levobupivacaine 27686-84-6,  
 Masoprocol 28395-03-1, Bumetanide 28657-80-9, Cinoxacin 28782-42-5,  
 Difenoxyol 28860-95-9, Carbidopa 28911-01-5, Triazolam 28981-97-7,  
 Alprazolam 29094-61-9, Glipizide 29110-47-2, Guanfacine 29122-68-7,  
 Atenolol 30516-87-1, Zidovudine 31441-78-8, Mercaptopurine  
 31677-93-7, Bupropion hydrochloride 31828-71-4, Mexiletine 31883-05-3,  
 Moricizine 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 33419-42-0,  
 Etoposide 34089-81-1, Sodium ferric gluconate 35189-28-7, Norgestimate  
 36322-90-4, Piroxicam 36505-84-7, Buspirone 36791-04-5, Ribavirin  
 38304-91-5, Minoxidil 40180-04-9, Tienilic acid 40580-59-4, Guanadrel  
 41575-94-4, Carboplatin 41708-72-9, Tocainide 42399-41-7, Diltiazem  
 42924-53-8, Nabumetone 49562-28-9, Fenofibrate 50679-08-8, Terfenadine  
 50925-79-6, Colestipol 50972-17-3, Bacampicillin 51022-71-0, Nabilone  
 51110-01-1, Somatostatin 51333-22-3, Budesonide 51384-51-1, Metoprolol  
 51481-61-9, Cimetidine 53179-11-6, Loperamide 53230-10-7, Mefloquine  
 53608-75-6, Pancrelipase 53714-56-0, Leuprolide 53994-73-3, Cefaclor  
 54024-22-5, Desogestrel 54063-53-5, Propafenone 54143-56-5, Flecainide  
 acetate 54182-58-0, Sucralfate 54350-48-0, Etretinate 54573-75-0,  
 Doxercalciferol 54910-89-3, Fluoxetine 55142-85-3, Ticlopidine  
 55268-75-2, Cefuroxime 55985-32-5, Niacardipine 56420-45-2, Epirubicin  
 58001-44-8 58581-89-8, Azelastine 59122-46-2, Misoprostol  
 59277-89-3, Acyclovir 59729-33-8, Citalopram 59865-13-3, Cyclosporine  
 A 60142-96-3, Gabapentin 60205-81-4, Ipratropium 61489-71-2,  
 Menotropin 61718-82-9, Fluvoxamine maleate 61869-08-7, Paroxetine

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62571-86-2, Captopril 63585-09-1, Foscarnet sodium 63590-64-7,  
Terazosin 64952-97-2, Latamoxef 65141-46-0, Nicorandil 65277-42-1,  
Ketoconazole 66085-59-4, Nimodipine 66104-22-1, Pergolide  
66357-35-5, Ranitidine 66376-36-1, Alendronate 67227-57-0, Fenoldopam  
mesylate 68475-42-3, Anagrelide 68844-77-9, Astemizole 69049-73-6,  
Nedocromil 69123-98-4, Fialuridine 69655-05-6, Didanosine  
70359-46-5, Brominide tartrate 70989-04-7, S-Mephenytoin 71320-77-9,  
Moclobemide 72432-03-2, Miglitol 72509-76-3, Felodipine 72956-09-3,  
Carvedilol 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74191-85-8,  
Doxazosin 75330-75-5, Lovastatin 75695-93-1, Isradipine 75706-12-6,  
Leflunomide 75847-73-3, Enalapril 76470-66-1, Loracarbef 76547-98-3,  
Lisinopril 76568-02-0, Flosequinan 76584-70-8 76824-35-6, Famotidine  
76932-56-4, Nafarelin 76963-41-2, Nizatidine 78110-38-0, Aztreonam  
78628-80-5, Terbinafine hydrochloride 79516-68-0, Levocabastine  
79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin  
80125-14-0, Remoxipride 80474-14-2, Fluticasone propionate 81093-37-0,  
Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin  
81669-57-0, Anistreplase 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin  
82626-48-0, Zolpidem 82834-16-0, Perindopril 83366-66-9, Nefazodone  
83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5,  
Azithromycin 84057-84-1, Lamotrigine 84449-90-1, Raloxifene  
84625-61-6, Itraconazole 85441-61-8, Quinapril 85721-33-1,  
Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril  
87333-19-5, Ramipril 87679-37-6, Trandolapril 88040-23-7, Cefepime  
88150-42-9, Amlodipine 89365-50-4, Salmeterol 89778-26-7, Toremifene  
90566-53-3, Fluticasone 91714-94-2, Bromfenac  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); BIOL (Biological study)

(methods of determining individual hypersensitivity to a pharmaceutical  
agent from gene expression profile)

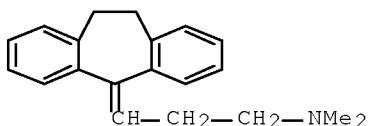
IT ~~50-48-6~~, Amitriptyline ~~10262-69-8~~, Maprotiline  
~~14028-44-5~~, Amoxapine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); BIOL (Biological study)

(methods of determining individual hypersensitivity to a pharmaceutical  
agent from gene expression profile)

RN 50-48-6 ZCAPLUS

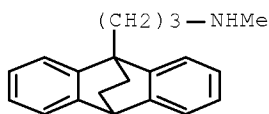
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-  
dimethyl- (CA INDEX NAME)



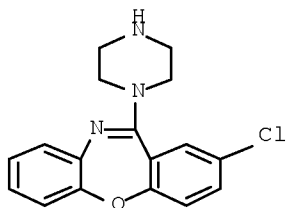
RN 10262-69-8 ZCAPLUS

CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)

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RN 14028-44-5 ZCAPLUS  
CN Dibenz[b,f][1,4]oxazepine, 2-chloro-11-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD  
(5 CITINGS)  
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 23 OF 49 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2003571445 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 14605211  
TITLE: Human targets of Pseudomonas aeruginosa pyocyanin.  
AUTHOR: Ran Huimin; Hassett Daniel J; Lau Gee W  
CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine,  
University of Cincinnati College of Medicine, 231 Albert  
Sabin Way, Cincinnati, OH 45267-0564, USA.  
SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America, (2003 Nov 25) Vol. 100, No. 24,  
pp. 14315-20. Electronic Publication: 2003-11-06.  
Journal code: 7505876. ISSN: 0027-8424.  
Report No.: NLM-PMC283589.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (IN VITRO)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200402  
ENTRY DATE: Entered STN: 16 Dec 2003  
Last Updated on STN: 3 Feb 2004  
Entered Medline: 2 Feb 2004

ABSTRACT:  
Pseudomonas aeruginosa produces copious amounts of the redoxactive tricyclic  
compound pyocyanin that kills competing microbes and mammalian cells,  
especially during cystic fibrosis lung infection. Cross-phylum  
susceptibility to pyocyanin suggests the existence of evolutionarily conserved

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physiological targets. We screened a *Saccharomyces cerevisiae* deletion library to identify presumptive pyocyanin targets with the expectation that similar targets would be conserved in humans. Fifty *S. cerevisiae* targets were provisionally identified, of which 60% have orthologous human counterparts. These targets encompassed major cellular pathways involved in the cell cycle, electron transport and respiration, epidermal cell growth, protein sorting, vesicle transport, and the vacuolar ATPase. Using cultured human lung epithelial cells, we showed that pyocyanin-mediated reactive oxygen intermediates inactivate human vacuolar ATPase, supporting the validity of the yeast screen. We discuss how the inactivation of V-ATPase may negatively impact the lung function of *cystic fibrosis* patients.

CONTROLLED TERM: Apoptosis: DE, drug effects  
Cell Line  
Drug Resistance, Fungal  
Electron Transport: DE, drug effects  
Genes, Bacterial  
Genes, Fungal: DE, drug effects  
Humans  
Oxidative Stress: DE, drug effects  
\**Pseudomonas aeruginosa*: PY, pathogenicity  
\*Pyocyanine: TO, toxicity  
\**Saccharomyces cerevisiae*: DE, drug effects  
*Saccharomyces cerevisiae*: GE, genetics  
*Saccharomyces cerevisiae*: ME, metabolism  
Sequence Deletion  
Vacuolar Proton-Translocating ATPases: GE, genetics  
Vacuolar Proton-Translocating ATPases: ME, metabolism  
CAS REGISTRY NO.: 85-66-5 (Pyocyanine)  
CHEMICAL NAME: EC 3.6.1.- (Vacuolar Proton-Translocating ATPases)

L91 ANSWER 24 OF 49 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2003474605 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 14550580  
TITLE: Benefits of different drug formulations in  
psychopharmacology.  
AUTHOR: Frijlink Henderik W  
CORPORATE SOURCE: Department of Pharmaceutical Technology and Biopharmacy,  
Groningen University Institute for Drug Exploration,  
Groningen, The Netherlands.. frijlink@farm.rug.nl  
SOURCE: European neuropsychopharmacology : the journal of the  
European College of Neuropsychopharmacology, (2003 Sep)  
Vol. 13 Suppl 3, pp. S77-84. Ref: 24  
Journal code: 9111390. ISSN: 0924-977X.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200311  
ENTRY DATE: Entered STN: 11 Oct 2003  
Last Updated on STN: 19 Dec 2003  
Entered Medline: 21 Nov 2003

ABSTRACT:  
Adequate dosage forms are essential for achieving successful pharmacotherapy. Innovative dosage forms or delivery systems may direct a drug to its specific site of action, optimize the timing of the drug release, or increase comfort or convenience for the patient. Thus, such innovations may improve efficacy and tolerability and lead to improvements in health-related quality of life. Specialized dosage forms (e.g., depot injections, extended-release formulations) of several psychiatric agents have been extensively used. The

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latest addition is an orally disintegrating formulation of the antidepressant mirtazapine. This dosage form dissolves rapidly in the mouth and is convenient for the large proportion of patients who have difficulty in swallowing tablets.

CONTROLLED TERM: Anti-Bacterial Agents: AD, administration & dosage  
\*Chemistry, Pharmaceutical  
Circadian Rhythm  
Cystic Fibrosis: DT, drug therapy  
Drug Administration Routes  
\*Drug Delivery Systems  
Humans  
Mianserin: AD, administration & dosage  
\*Mianserin: AA, analogs & derivatives  
Mianserin: ME, metabolism  
Patient Compliance  
Proton Pumps: AD, administration & dosage  
Proton Pumps: AI, antagonists & inhibitors  
\*Psychopharmacology  
CAS REGISTRY NO.: 24219-97-4 (Mianserin); 61337-67-5 (mirtazapine)  
CHEMICAL NAME: 0 (Anti-Bacterial Agents); 0 (Proton Pumps)

L91 ANSWER 25 OF 49 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 1993192191 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 8448110  
TITLE: Sequence-selective binding of amiloride to DNA.  
AUTHOR: Bailly C; Cuthbert A W; Gentle D; Knowles M R; Waring M J  
CORPORATE SOURCE: Department of Pharmacology, University of Cambridge, U.K.  
SOURCE: Biochemistry, (1993 Mar 16) Vol. 32, No. 10, pp. 2514-24.  
Journal code: 0370623. ISSN: 0006-2960.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199304  
ENTRY DATE: Entered STN: 23 Apr 1993  
Last Updated on STN: 3 Feb 1997  
Entered Medline: 13 Apr 1993

ABSTRACT:

Nuclease footprinting techniques have been employed to investigate the interaction between the diuretic drug amiloride, a sodium channel blocker with potential therapeutic use in the treatment of cystic fibrosis, and three DNA fragments of defined sequence. Using either DNase I or micrococcal nuclease as probes, an unusual pattern of sequence-selective recognition of DNA has been detected. Amiloride binds selectively to sites rich in adenine and thymine residues, frequently with an apparent preference for 5'-TpX-3' steps, and discriminates strongly against GC-rich sequences which are sometimes cut more readily in the presence of the drug compared to the control. A detailed comparison with the actions of known selective DNA-binding antibiotics and drugs reveals a unique pattern of binding sites, different from those of typical intercalators on the one hand and those of minor groove-binders on the other. Amiloride is believed to adopt a pH-dependent tricyclic hydrogen-bonded conformation in solution which allows it to intercalate into DNA; consistent with this belief, we find that the footprinting pattern largely disappears at pH values above the pKa. Preliminary studies with three amiloride analogues have indicated the importance of two functional groups in the recognition of DNA. The possible relevance of selective DNA binding to activity in vivo is considered.

CONTROLLED TERM: \*Amiloride: CH, chemistry

Base Sequence  
 Binding Sites  
 \*DNA: CH, chemistry  
 \*DNA, Bacterial: CH, chemistry  
 Deoxyribonuclease I  
 Escherichia coli: GE, genetics  
 \*Intercalating Agents  
 Kinetics  
 Molecular Sequence Data  
 \*Oligodeoxyribonucleotides: CH, chemistry  
 Plasmids  
 Promoter Regions, Genetic  
 RNA, Transfer, Tyr: GE, genetics  
 CAS REGISTRY NO.: 2609-46-3 (Amiloride); 9007-49-2 (DNA)  
 CHEMICAL NAME: 0 (DNA, Bacterial); 0 (Intercalating Agents); 0  
 (Oligodeoxyribonucleotides); 0 (RNA, Transfer, Tyr); 0  
 (T-DNA); EC 3.1.21.1 (Deoxyribonuclease I)  
 GENE NAME: tyr

L91 ANSWER 26 OF 49 MEDLINE on STN  
 ACCESSION NUMBER: 2004554886 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 15526520  
 TITLE: Pulmonary involvement in diabetes mellitus.  
 AUTHOR: Nicolaie T; Zavoianu Cristina; Nuta P  
 CORPORATE SOURCE: 2nd Clinic of Internal Medicine, Central Emergency Clinic  
 Military Hospital, Bucharest, Romania..  
 nicolaiee8@yahoo.com  
 SOURCE: Romanian journal of internal medicine = Revue roumaine de  
 medecine interne, (2003) Vol. 41, No. 4, pp. 365-74.  
 Ref: 44  
 Journal code: 9304507. ISSN: 1220-4749.  
 PUB. COUNTRY: Romania  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200411  
 ENTRY DATE: Entered STN: 6 Nov 2004  
 Last Updated on STN: 20 Dec 2004  
 Entered Medline: 30 Nov 2004

## ABSTRACT:

Diabetes mellitus involves the lungs in the course of the complex phenomena it generates. Recent research in animal diabetes as well as in human diabetes demonstrated biochemical changes at the pulmonary level such as the suppression of anyline p-hydroxylase, the reduction of the activity of glutathione-peroxidase, the development of NO-dependent endothelial dysfunction, microsomal disorders, increased heparan sulphate at the level of the vascular basement membrane, increased levels of advanced glycation end-products and the derangement of bronchial mucus production by amyline. Structural modifications of the lung parenchyma were observed such as the narrowing of the alveolar space, the flattening of the alveolar epithelium and the expansion of the interstitium. Aside from the involvement of the pulmonary vessels there is the involvement of the basement membranes of the alveolar epithelium, the bronchial epithelium and the pulmonary capillaries. The consequences of local oxidative stress, the increased vascular permeability and the modifications in mucus secretion lead to the reduction of pulmonary volumes, pulmonary diffusion capacity, elastic recoil with involvement of restrictive lung disorders, diminished bronchial reactivity and diminished bronchodilatation. Data of pulmonary pathology obtained from patients as well as pulmonary involvement of children born of diabetic mothers are presented

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succinctly.

CONTROLLED TERM:       Animals  
                          Basement Membrane: PA, pathology  
                          Cystic Fibrosis: CO, complications  
                          Diabetes Complications  
                          \*Diabetes Mellitus: PA, pathology  
                          \*Diabetes Mellitus: PP, physiopathology  
                          Endothelium, Vascular: PA, pathology  
                          Glycosylation End Products, Advanced: ME, metabolism  
                          Humans  
                          \*Lung: PA, pathology  
                          Lung Diseases: PA, pathology  
                          Lung Diseases: PP, physiopathology  
                          Pulmonary Alveoli: PA, pathology  
                          Pulmonary Alveoli: PP, physiopathology  
                          Respiratory Tract Infections: PA, pathology  
                          Respiratory Tract Infections: PP, physiopathology  
CHEMICAL NAME:       0 (Glycosylation End Products, Advanced)

L91 ANSWER 27 OF 49       MEDLINE on STN  
ACCESSION NUMBER:   1983307213       MEDLINE   Full-text  
DOCUMENT NUMBER:    PubMed ID: 6764592  
TITLE:               [Iatrogenic pathology of the optic nerve].  
                      Pathologie iatrogene du nerf optique.  
AUTHOR:             Hamard H; Desbordes J M  
SOURCE:             L'Annee therapeutique et clinique en ophtalmologie,  
                      (1982) Vol. 33, pp. 185-202. Ref: 27  
                      Journal code: 0405351. ISSN: 0301-4495.  
                      Report No.: PIP-019579; POP-00131382.  
PUB. COUNTRY:       France  
DOCUMENT TYPE:       (ENGLISH ABSTRACT)  
                      Journal; Article; (JOURNAL ARTICLE)  
                      General Review; (REVIEW)  
LANGUAGE:           French  
FILE SEGMENT:       Priority Journals; Population  
ENTRY MONTH:        198310  
ENTRY DATE:          Entered STN: 19 Mar 1990  
                      Last Updated on STN: 1 Nov 2002  
                      Entered Medline: 8 Oct 1983

ABSTRACT:

Iatrogenic pathology of the optic nerve is examined according to a framework which distinguishes direct and indirect effects on the optic nerve. Direct effects due to toxic drugs should be suspected when unexplained, usually bilateral loss of visual acuity occurs. The 3 clinical stages of classical optic toxic neuropathy are 1) anomalies of color vision, 2) loss of visual acuity and narrowing field of vision, and 3) papillary palor corresponding to irreversible optic atrophy. Usually only the 1st stages are reversible, but the reversibility may be incomplete. The list of drugs which can cause such effects is lengthy and includes antiinfectious drugs such as sulfamides and derivatives of hydroxyquinoleins, chloramphenicol especially when used to treat cystic fibrosis of the pancreas in children, the antituberculins ethambutol in high doses and isoniazide, which occasion particular risks when combined; antiparasitics such as quinine and its derivatives chloroquine and hydroxychloroquine, which cause optic neuropathy through their effect on the retina; arsenic pentavalents such as tryparsamide, quinacrine, trecator and mystatin; drugs affecting the central nervous system such as monoamineoxydase inhibitors, laroxyll, phenothiazine and the barbituates; anticonvulsants such as phenytoin; antimitotics such as vincristine, digitalics, disulfiram; penicillamines, and pexid. The action of lasers on the optic nerve can have a similar effect. The optic nerve may be indirectly damaged during surgical

procedures leading to hypotonia, acute ischemia of the head of the optic nerve or embolic accident after a local or regional injection. Damage may also be caused by radiotherapy of intracranial tumors and certain drugs which cause isolated papillary edema or edema associated with headaches, such as Tetracycline, large doses of vitamin A or D, corticoids, and oral contraceptive (OC) pills, which may cause papillary edema through cerebral pseudo-tumors that regress with discontinuation of treatment. This condition has been observed in women with uncontrolled hyperlipidemia. It is probable that an alteration of axonal transport is at the basis of the neuropathic mechanisms. The 1st step in therapy is the suppression of the toxin, or at least its discontinuation. Some success has been obtained with vitamin B therapy, corticotherapy, zinc, or isaxoxine, depending on the specific condition.

SUPPLEMENTARY TERM: Biology; Central Nervous System Effects; Contraception; Contraceptive Agents; Contraceptive Agents, Female; Contraceptive Methods--side effects; Drugs; Family Planning; Headache; Lipid Metabolic Effects; Ophthalmological Effects; Oral Contraceptives--side effects; Physiology; Reproductive Control Agents; Treatment

CONTROLLED TERM: Check Tags: Female  
 Adrenal Cortex Hormones: AE, adverse effects  
 Antiprotozoal Agents: AE, adverse effects  
 Chloramphenicol: AE, adverse effects  
 Contraceptives, Oral: AE, adverse effects  
 Ethambutol: AE, adverse effects  
 Humans  
 Iatrogenic Disease  
 Isoniazid: AE, adverse effects  
 Monoamine Oxidase Inhibitors: AE, adverse effects  
 \*Optic Nerve Diseases: ET, etiology  
 Optic Nerve Diseases: TH, therapy  
 Phenytoin: AE, adverse effects  
 Quinine: AA, analogs & derivatives  
 Radiotherapy: AE, adverse effects  
 Surgical Procedures, Operative: AE, adverse effects  
 Vitamins: AE, adverse effects

CAS REGISTRY NO.: 130-95-0 (Quinine); 54-85-3 (Isoniazid); 56-75-7 (Chloramphenicol); 57-41-0 (Phenytoin); 74-55-5 (Ethambutol)

CHEMICAL NAME: 0 (Adrenal Cortex Hormones); 0 (Antiprotozoal Agents); 0 (Contraceptives, Oral); 0 (Monoamine Oxidase Inhibitors); 0 (Vitamins)

L91 ANSWER 28 OF 49 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003500456 EMBASE Full-text  
 TITLE: Human targets of *Pseudomonas aeruginosa* pyocyanin.  
 AUTHOR: Ran, Huimin; Lau, Gee W. (correspondence)  
 CORPORATE SOURCE: Div. of Pulmon./Critical Care Med., Univ. of Cincinnati Coll. of Med., 231 Albert Sabin Way, Cincinnati, OH 45267-0564, United States. gee.lau@uc.edu  
 AUTHOR: Hassett, Daniel J.  
 CORPORATE SOURCE: Department of Molecular Genetics, Univ. of Cincinnati Coll. of Med., 231 Albert Sabin Way, Cincinnati, OH 45267-0564, United States.  
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (25 Nov 2003) Vol. 100, No. SUPPL. 2, pp. 14315-14320.  
 Refs: 63  
 ISSN: 0027-8424 CODEN: PNASA6  
 COUNTRY: United States



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DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology  
and Virology

LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 5 Jan 2004  
Last Updated on STN: 5 Jan 2004

ABSTRACT: *Pseudomonas aeruginosa* produces copious amounts of the redoxactive tricyclic compound pyocyanin that kills competing microbes and mammalian cells, especially during cystic fibrosis lung infection. Cross-phylum susceptibility to pyocyanin suggests the existence of evolutionarily conserved physiological targets. We screened a *Saccharomyces cerevisiae* deletion library to identify presumptive pyocyanin targets with the expectation that similar targets would be conserved in humans. Fifty S. cerevisiae targets were provisionally identified, of which 60% have orthologous human counterparts. These targets encompassed major cellular pathways involved in the cell cycle, electron transport and respiration, epidermal cell growth, protein sorting, vesicle transport, and the vacuolar ATPase. Using cultured human lung epithelial cells, we showed that pyocyanin-mediated reactive oxygen intermediates inactivate human vacuolar ATPase, supporting the validity of the yeast screen. We discuss how the inactivation of V-ATPase may negatively impact the lung function of cystic fibrosis patients.

CONTROLLED TERM: Medical Descriptors:  
animal cell  
article  
calcium homeostasis  
cell killing  
cystic fibrosis  
DNA library  
electron transport  
gene deletion  
genetic susceptibility  
hospital infection  
lung function  
microbial growth  
nonhuman  
oxidation reduction reaction  
priority journal  
\**Pseudomonas aeruginosa*  
*Saccharomyces cerevisiae*  
\*target cell

CONTROLLED TERM: Drug Descriptors:  
\*pyocyanine  
CAS REGISTRY NO.: (pyocyanine) 85-66-5

L91 ANSWER 29 OF 49 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003351713 EMBASE Full-text

TITLE: Ciprofloxacin-induced renal insufficiency in cystic fibrosis.

AUTHOR: Moffett, Brady S.

CORPORATE SOURCE: Department of Pharmacy, Johns Hopkins Medical Institutions, 600 N. Wolfe Street, Park 316, Baltimore, MD 21287, United States.

AUTHOR: Rosenstein, Beryl J.; Mogayzel Jr., Peter J.  
(correspondence)

CORPORATE SOURCE: Eudowood Div. Pediatric Resp. Sci., Johns Hopkins Medical Institutions, 600 N. Wolfe Street, Park 316, Baltimore, MD 21287, United States. mogayzel@mail.jhmi.edu

10/524815

AUTHOR: Moffett, Brady S.  
CORPORATE SOURCE: Texas Children's Hospital, Department of Pharmacy, 6621  
Fannin Street, Houston, TX 77030, United States.  
SOURCE: Journal of Cystic Fibrosis, (Sep 2003) Vol. 2, No. 3, pp.  
152-154.  
Refs: 15  
ISSN: 1569-1993 CODEN: JCFOAC  
PUBLISHER IDENT.: S 1569-1993(03)00059-6  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
028 Urology and Nephrology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
004 Microbiology: Bacteriology, Mycology, Parasitology  
and Virology  
048 Gastroenterology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 11 Sep 2003  
Last Updated on STN: 11 Sep 2003

ABSTRACT: Acute renal insufficiency is known to occur in patients who are taking ciprofloxacin, particularly the elderly. We report two young patients with cystic fibrosis who presented with acute renal insufficiency after 2-3 weeks of oral ciprofloxacin therapy. The incidence of this adverse effect in children and young adults who have cystic fibrosis is unknown. Multiple mechanisms for ciprofloxacin-induced nephrotoxicity have been proposed.  
.COPYRGT. 2003 European Cystic Fibrosis Society. Published by Elsevier Science B.V. All rights reserved.

CONTROLLED TERM: Medical Descriptors:  
\*acute kidney failure: SI, side effect  
adolescent  
adult  
anorexia: SI, side effect  
article  
case report  
\*cystic fibrosis  
drug induced disease: SI, side effect  
echography  
elderly care  
female  
human  
incidence  
laboratory test  
lung infection: DT, drug therapy  
Mycobacterium intracellulare avium  
nausea: SI, side effect  
nephrotoxicity: SI, side effect  
Pseudomonas aeruginosa  
Stenotrophomonas maltophilia  
symptomatology  
urinalysis  
vomiting: SI, side effect

CONTROLLED TERM: Drug Descriptors:  
aminoglycoside antibiotic agent: DT, drug therapy  
aminoglycoside antibiotic agent: IV, intravenous drug  
administration  
azithromycin: DT, drug therapy  
\*ciprofloxacin: AE, adverse drug reaction

\*ciprofloxacin: CB, drug combination  
 \*ciprofloxacin: DT, drug therapy  
 \*ciprofloxacin: PO, oral drug administration  
 clarithromycin: CB, drug combination  
 clarithromycin: DT, drug therapy  
 cotrimoxazole: DT, drug therapy  
 dornase alfa: DT, drug therapy  
 ethambutol: AE, adverse drug reaction  
 ethambutol: CB, drug combination  
 ethambutol: DT, drug therapy  
 fluticasone propionate plus salmeterol  
 isoniazid: AE, adverse drug reaction  
 isoniazid: CB, drug combination  
 isoniazid: DT, drug therapy  
 nortriptyline  
 omeprazole: DT, drug therapy  
 pancreas enzyme: DT, drug therapy  
 pyridoxine: CB, drug combination  
 pyridoxine: DT, drug therapy  
 rifabutin: AE, adverse drug reaction  
 rifabutin: CB, drug combination  
 rifabutin: DT, drug therapy  
 salbutamol  
 theophylline  
 tobramycin: DT, drug therapy  
 tobramycin: IH, inhalational drug administration  
 vitamin

CAS REGISTRY NO.: (azithromycin) 83905-01-5; (ciprofloxacin) 85721-33-1;  
 (clarithromycin) 81103-11-9; (cotrimoxazole) 8064-90-2;  
 (dornase alfa) 143831-71-4; (ethambutol) 10054-05-4,  
 1070-11-7, 3577-94-4, 74-55-5; (isoniazid) 54-85-3,  
 62229-51-0, 65979-32-0; (nortriptyline) 72-69-5,  
 894-71-3; (omeprazole) 73590-58-6, 95510-70-6; (pyridoxine)  
 12001-77-3, 58-56-0, 65-23-6, 8059-24-3; (rifabutin)  
 72559-06-9; (salbutamol) 18559-94-9; (theophylline)  
 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9;  
 (tobramycin) 32986-56-4

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ACCESSION NUMBER: 2003396282 EMBASE Full-text  
 TITLE: Benefits of different drug formulations in  
 psychopharmacology.  
 AUTHOR: Frijlink, Henderik W. (correspondence)  
 CORPORATE SOURCE: Dept. Pharmaceutical Technol./B., Groningen Univ. Inst.  
 Drug Explor., Groningen, Netherlands. frijlink@farm.rug.nl  
 SOURCE: European Neuropsychopharmacology, (Sep 2003) Vol. 13, No.  
 SUPPL. 3, pp. S77-S84.  
 Refs: 24  
 ISSN: 0924-977X CODEN: EURNE8  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)  
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology  
 032 Psychiatry  
 037 Drug Literature Index  
 039 Pharmacy  
 006 Internal Medicine  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 16 Oct 2003

Last Updated on STN: 16 Oct 2003

ABSTRACT: Adequate dosage forms are essential for achieving successful pharmacotherapy. Innovative dosage forms or delivery systems may direct a drug to its specific site of action, optimize the timing of the drug release, or increase comfort or convenience for the patient. Thus, such innovations may improve efficacy and tolerability and lead to improvements in health-related quality of life. Specialized dosage forms (e.g., depot injections, extended-release formulations) of several psychiatric agents have been extensively used. The latest addition is an orally disintegrating formulation of the antidepressant ~~mirtazapine~~. This dosage form dissolves rapidly in the mouth and is convenient for the large proportion of patients who have difficulty in swallowing tablets. .COPYRG. 2003 Elsevier B.V./ECNP. All rights reserved.

CONTROLLED TERM: Medical Descriptors:  
 allergy  
 asthma  
 bioequivalence  
 cancer  
 chronic obstructive lung disease  
 chronotherapy  
 circadian rhythm  
 circadian rhythm sleep disorder  
 conference paper  
 congestive heart failure  
 cystic fibrosis: DT, drug therapy  
 cystic fibrosis: EP, epidemiology  
 cystic fibrosis: PC, prevention  
 diabetes mellitus: DT, drug therapy  
 drug absorption  
 drug delivery system  
 drug dosage form  
 \*drug formulation  
 drug release  
 epilepsy  
 glaucoma  
 human  
 Human immunodeficiency virus infection  
 hyperlipidemia  
 hypertension: DT, drug therapy  
 immunosuppressive treatment  
 infection prevention  
 inhaler  
 kidney transplantation  
 medical nebulizer  
 mental disease: DT, drug therapy  
 nebulization  
 patient compliance  
 peptic ulcer  
 postmenopause  
 priority journal  
 \*psychopharmacology  
 quality of life  
 rheumatoid arthritis  
 tuberculosis

CONTROLLED TERM: Drug Descriptors:  
 amfebutamone: DT, drug therapy  
 amfebutamone: PR, pharmaceuticals  
 antibiotic agent: DT, drug therapy  
 antibiotic agent: IH, inhalational drug administration

antibiotic agent: PR, pharmaceuticals  
 antidepressant agent: DT, drug therapy  
 antidepressant agent: PO, oral drug administration  
 antidepressant agent: PR, pharmaceuticals  
 antidepressant agent: PK, pharmacokinetics  
 calcium channel blocking agent: DT, drug therapy  
 calcium channel blocking agent: PR, pharmaceuticals  
 colistin: DT, drug therapy  
 colistin: IH, inhalational drug administration  
 colistin: PR, pharmaceuticals  
 ethinylestradiol plus etonogestrel: PR, pharmaceuticals  
 etonogestrel: PR, pharmaceuticals  
 flupentixol: DT, drug therapy  
 flupentixol: PR, pharmaceuticals  
 fluphenazine: DT, drug therapy  
 fluphenazine: PR, pharmaceuticals  
 gestagen: PR, pharmaceuticals  
 haloperidol: DT, drug therapy  
 haloperidol: PR, pharmaceuticals  
 immunosuppressive agent  
 insulin: DT, drug therapy  
 insulin: IH, inhalational drug administration  
 insulin: PR, pharmaceuticals  
 insulin: SC, subcutaneous drug administration  
 levonorgestrel: PR, pharmaceuticals  
 mirtazapine: DT, drug therapy  
 mirtazapine: PO, oral drug administration  
 mirtazapine: PR, pharmaceuticals  
 mirtazapine: PK, pharmacokinetics  
 mirtrazapine soltab  
 omeprazole: PO, oral drug administration  
 omeprazole: PR, pharmaceuticals  
 proton pump inhibitor: PO, oral drug administration  
 proton pump inhibitor: PR, pharmaceuticals  
 serotonin uptake inhibitor: DT, drug therapy  
 serotonin uptake inhibitor: PR, pharmaceuticals  
 tobramycin: DT, drug therapy  
 tobramycin: IH, inhalational drug administration  
 tobramycin: PR, pharmaceuticals  
 venlafaxine: DT, drug therapy  
 venlafaxine: PO, oral drug administration  
 venlafaxine: PR, pharmaceuticals  
 verapamil: DT, drug therapy  
 verapamil: PR, pharmaceuticals

CAS REGISTRY NO.: (amfebutamone) 31677-93-7, 34911-55-2; (colistin) 1066-17-7, 1264-72-8; (etonogestrel) 54048-10-1; (flupentixol) 2413-38-9, 2709-56-0; (fluphenazine) 146-56-5, 69-23-8; (haloperidol) 52-86-8; (insulin) 9004-10-8; (levonorgestrel) 797-63-7; (mirtazapine) 61337-67-5; (omeprazole) 73590-58-6, 95510-70-6; (tobramycin) 32986-56-4; (venlafaxine) 93413-69-5; (verapamil) 152-11-4, 52-53-9  
 CHEMICAL NAME: (1) implanon; (2) mirena; (3) nuvaring; implanon; mirena  
 COMPANY NAME: (1) Organon; (2) Schering; (3) Organon

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ACCESSION NUMBER: 2002335727 EMBASE Full-text  
 TITLE: Rofecoxib-induced instant aquagenic wrinkling of the palms.  
 AUTHOR: Carder, K. Robin; Weston, William L., Dr. (correspondence)

10/524815

CORPORATE SOURCE: Department of Dermatology, Univ. of CO Health Sciences Center, Box B-153, 4200 E. 9th Ave., Denver, CO 80262, United States. william.weston@uchsc.edu

SOURCE: Pediatric Dermatology, (Jul 2002) Vol. 19, No. 4, pp. 353-355.

Refs: 12

ISSN: 0736-8046 CODEN: PEDRDQ

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 013 Dermatology and Venereology  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 10 Oct 2002

Last Updated on STN: 10 Oct 2002

ABSTRACT: An 18-year-old woman presented with a 3-week complaint of exaggerated palmar wrinkling and swelling following brief exposure (1-2 minutes) of her hands to water. She had a history of mixed connective tissue disease and had been started on rofecoxib therapy 1 month prior to the onset of her skin symptoms. Discontinuation of rofecoxib was followed by resolution of symptoms within a period of 3 weeks. Similar palmar skin changes following water exposure have been reported to occur in *cystic fibrosis* and are thought to be due to increased salt content of the skin and secondary increased water-binding capacity. Rofecoxib is a selective COX-2 inhibitor that has been shown to increase sodium reabsorption in the kidney via effects on prostaglandin E2 and the renal vasculature. The COX-2 protein is also expressed in keratinocytes and plays a role in keratinocyte differentiation. Prostaglandin E2 also plays a role in keratinocyte proliferation and differentiation. Thus rofecoxib may cause increased sodium reabsorption in the skin, as it does in the kidney. The rofecoxib-associated elevation in skin sodium may increase keratin water-binding capacity and cause exaggerated aquagenic wrinkling of the skin, as occurs in *cystic fibrosis*.

CONTROLLED TERM: Medical Descriptors:  
adult  
article  
case report  
cell differentiation  
cell proliferation  
connective tissue disease: DT, drug therapy  
*cystic fibrosis*  
differential diagnosis  
drug mechanism  
drug withdrawal  
female  
human  
hydrophilicity  
keratinocyte  
\*palmar dermatoglyphics  
priority journal  
protein expression  
\*skin manifestation: SI, side effect  
sodium absorption  
water immersion

CONTROLLED TERM: Drug Descriptors:  
*amitriptyline*  
loratadine  
methotrexate: DT, drug therapy

methotrexate: IM, intramuscular drug administration  
 naproxen  
 nifedipine  
 pantoprazole  
 ranitidine

\*rofecoxib: AE, adverse drug reaction

\*rofecoxib: DT, drug therapy

\*rofecoxib: PD, pharmacology

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (loratadine)  
 79794-75-5; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5;  
 (naproxen) 22204-53-1, 26159-34-2; (nifedipine) 21829-25-4;  
 (pantoprazole) 102625-70-7; (ranitidine) 66357-35-5,  
 66357-59-3; (rofecoxib) 162011-90-7, 186912-82-3

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ACCESSION NUMBER: 2001380111 EMBASE Full-text

TITLE: Antioxidants: An integrative approach.

AUTHOR: Lachance, Paul A., Dr. (correspondence); Nakat, Zeina;  
 Jeong, Woo-Sik

CORPORATE SOURCE: Nutraceuticals Institute, Department of Food Science,  
 Rutgers, State University of New Jersey, New Brunswick, NJ,  
 United States. lachance@aesop.rutgers.edu

AUTHOR: Lachance, Paul A., Dr. (correspondence)

CORPORATE SOURCE: Nutraceuticals Institute, Department of Food Science,  
 Rutgers, State University of New Jersey, 65 Dudley Road,  
 New Brunswick, NJ 08901-8520, United States. lachance@aesop.  
 .rutgers.edu

AUTHOR: Lachance, Paul A., Dr. (correspondence)

CORPORATE SOURCE: Nutraceuticals Institute, Department of Food Science, State  
 University of New Jersey, 65 Dudley Road, New Brunswick, NJ  
 08901-8520, United States. lachance@aesop.rutgers.edu

SOURCE: Nutrition, (2001) Vol. 17, No. 10, pp. 835-838.

Refs: 46

ISSN: 0899-9007 CODEN: NUTRER

PUBLISHER IDENT.: S 0899-9007(01)00636-0

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

016 Cancer

029 Clinical and Experimental Biochemistry

046 Environmental Health and Pollution Control

LANGUAGE: English

ENTRY DATE: Entered STN: 15 Nov 2001

Last Updated on STN: 15 Nov 2001

CONTROLLED TERM: Medical Descriptors:

adult respiratory distress syndrome

aging

\*antioxidant activity

asthma

cancer

cardiovascular disease

cell function

chronic bronchitis

chronic obstructive lung disease

cigarette smoking

cystic fibrosis

diet supplementation

electron transport

emphysema

human  
immunity  
lipid peroxidation  
lung fibrosis  
mineral dust  
\*oxidative stress  
physical stress  
pneumonia  
priority journal  
review

CONTROLLED TERM: Drug Descriptors:  
\*alpha tocopherol  
amine oxidase (flavin containing): EC, endogenous compound  
~~amitriptyline~~  
asbestos  
ascorbic acid  
beta carotene  
catalase: EC, endogenous compound  
ciprofloxacin  
cyclosporin A  
cytochrome c oxidase: EC, endogenous compound  
\*free radical  
glutathione  
glutathione peroxidase: EC, endogenous compound  
hydrogen peroxide  
~~imipramine~~  
nitric oxide  
nitrogen dioxide  
oxygen radical  
ozone  
paracetamol  
polychlorinated biphenyl  
reactive oxygen metabolite  
scavenger  
superoxide dismutase: EC, endogenous compound  
tamoxifen  
xanthine oxidase: EC, endogenous compound

CAS REGISTRY NO.: (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4,  
58-95-7, 59-02-9; (amine oxidase (flavin containing))  
37255-42-8, 9001-66-5, 9059-11-4; (~~amitriptyline~~)  
~~50-48-6, 549-18-8~~; (asbestos) 1332-21-4; (ascorbic  
acid) 134-03-2, 15421-15-5, 50-81-7; (beta carotene)  
7235-40-7; (catalase) 9001-05-2; (ciprofloxacin)  
85721-33-1; (cyclosporin A) 59865-13-3, 63798-73-2;  
(cytochrome c oxidase) 72841-18-0, 9001-16-5; (glutathione  
peroxidase) 9013-66-5; (glutathione) 70-18-8; (hydrogen  
peroxide) 7722-84-1; (~~imipramine~~) ~~113-52-0, 50-49-7~~;  
(nitric oxide) 10102-43-9; (nitrogen dioxide) 10102-44-0;  
(ozone) 10028-15-6; (paracetamol) 103-90-2; (superoxide  
dismutase) 37294-21-6, 9016-01-7, 9054-89-1; (tamoxifen)  
10540-29-1; (xanthine oxidase) 9002-17-9

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ACCESSION NUMBER: 2000090698 EMBASE Full-text

TITLE: PharmaCE test questions.

SOURCE: Annals of Pharmacotherapy, (2000) Vol. 34, No. 3, pp. 413.  
ISSN: 1060-0280 CODEN: APhRER

COUNTRY: United States

DOCUMENT TYPE: Journal; Note



10/524815

FILE SEGMENT: 032 Psychiatry  
037 Drug Literature Index  
038 Adverse Reactions Titles  
007 Pediatrics and Pediatric Surgery

LANGUAGE: English

ENTRY DATE: Entered STN: 23 Mar 2000  
Last Updated on STN: 23 Mar 2000

CONTROLLED TERM: Medical Descriptors:  
\*antibiotic therapy  
clinical feature  
cystic fibrosis  
drug contraindication  
drug disposition  
drug indication  
drug induced disease: ET, etiology  
drug induced disease: SI, side effect  
drug research  
external otitis: DT, drug therapy  
group therapy  
human  
nightmare: DT, drug therapy  
note  
otitis media: DT, drug therapy  
\*posttraumatic stress disorder: DI, diagnosis  
\*posttraumatic stress disorder: DT, drug therapy  
\*posttraumatic stress disorder: TH, therapy  
priority journal  
\*psychopharmacotherapy  
rating scale  
salmonellosis: DT, drug therapy

CONTROLLED TERM: Drug Descriptors:  
amfebutamone: DT, drug therapy  
amitriptyline: DT, drug therapy  
\*antidepressant agent: DT, drug therapy  
buspirone: DT, drug therapy  
ciprofloxacin: AE, adverse drug reaction  
ciprofloxacin: DT, drug therapy  
ciprofloxacin: PK, pharmacokinetics  
clonazepam: DT, drug therapy  
clozapine: DT, drug therapy  
cyproheptadine: DT, drug therapy  
desipramine: DT, drug therapy  
fluoxetine: DT, drug therapy  
fluvoxamine: DT, drug therapy  
guanfacine: DT, drug therapy  
imipramine: DT, drug therapy  
lithium: DT, drug therapy  
nefazodone: DT, drug therapy  
ofloxacin: AE, adverse drug reaction  
ofloxacin: DT, drug therapy  
ofloxacin: PK, pharmacokinetics  
paroxetine: DT, drug therapy  
pefloxacin: AE, adverse drug reaction  
pefloxacin: DT, drug therapy  
pefloxacin: PK, pharmacokinetics  
propranolol: DT, drug therapy  
\*quinoline derived antiinfective agent: AE, adverse drug  
reaction  
\*quinoline derived antiinfective agent: DT, drug therapy  
\*quinoline derived antiinfective agent: PK,

pharmacokinetics

risperidone: DT, drug therapy

valproic acid: DT, drug therapy

CAS REGISTRY NO.: (amfebutamone) 31677-93-7, 34911-55-2; (amitriptyline) 50-48-6, 549-18-8; (buspirone) 33386-08-2, 36505-84-7; (ciprofloxacin) 85721-33-1; (clonazepam) 1622-61-3; (clozapine) 5786-21-0; (cyproheptadine) 129-03-3, 969-33-5; (desipramine) 50-47-5, 58-28-6; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine) 54739-18-3; (guanfacine) 29110-47-2, 29110-48-3; (imipramine) 113-52-0, 50-49-7; (lithium) 7439-93-2; (nefazodone) 82752-99-6, 83366-66-9; (ofloxacin) 82419-36-1; (paroxetine) 61869-08-7; (pefloxacin) 70458-92-3; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (risperidone) 106266-06-2; (valproic acid) 1069-66-5, 99-66-1

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ACCESSION NUMBER: 2004314067 EMBASE Full-text

TITLE: Microvascular complications in cystic fibrosis-related diabetes mellitus: A case report.

AUTHOR: Scott, Andrew I.R.; Bell, Scott C. (correspondence)

CORPORATE SOURCE: Adult Cystic Fibrosis Unit, University of Queensland, Rode Rd., Brisbane, QLD 4032, Australia. bells@health.qld.gov.au

AUTHOR: Clarke, Belinda E.

CORPORATE SOURCE: Department of Anatomical Pathology, The Prince Charles Hospital, Brisbane, QLD, Australia.

AUTHOR: Healy, Helen

CORPORATE SOURCE: Department of Renal Medicine, Royal Brisbane Hospital, Brisbane, QLD, Australia.

AUTHOR: D'Emden, Michael

CORPORATE SOURCE: Department of Endocrinology, Royal Brisbane Hospital, Brisbane, QLD, Australia.

AUTHOR: Bell, Scott C. (correspondence)

CORPORATE SOURCE: Department of Thoracic Medicine, University of Queensland, The Prince Charles Hospital, Rode Rd., Brisbane, QLD 4032, Australia. bells@health.qld.gov.au

SOURCE: Journal of the Pancreas, (Nov 2000) Vol. 1, No. 4, pp. 208-210.

Refs: 6

ISSN: 1590-8577 CODEN: JPOAC6

COUNTRY: Italy

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
048 Gastroenterology  
006 Internal Medicine

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 5 Aug 2004

Last Updated on STN: 5 Aug 2004

ABSTRACT: Context. The prevalence of cystic fibrosis-related diabetes mellitus is increasing and is associated with increased survival from cystic fibrosis. Case Report. This study describes a case of the premature onset of disabling and widespread microvascular complications resulting from cystic fibrosis-related diabetes mellitus. Previously asymptomatic retinopathy was diagnosed on recognition of diabetic nephropathy. Conclusions. The treatment of pulmonary exacerbations has become more complex due to the nephrotoxic

10/524815

potential of intravenous aminoglycoside drugs which are frequently used to control chronic Pseudomonas infection in cystic fibrosis.

CONTROLLED TERM: Medical Descriptors:

adult  
article  
case report  
\*cystic fibrosis: DI, diagnosis  
\*cystic fibrosis: DT, drug therapy  
\*diabetes mellitus: CO, complication  
\*diabetes mellitus: DI, diagnosis  
\*diabetes mellitus: DT, drug therapy  
\*diabetes mellitus: PC, prevention  
\*diabetes mellitus: TH, therapy  
\*diabetic angiopathy: CO, complication  
\*diabetic angiopathy: ET, etiology  
diabetic nephropathy: CO, complication  
diabetic nephropathy: DI, diagnosis  
diabetic nephropathy: DT, drug therapy  
diabetic retinopathy: CO, complication  
diabetic retinopathy: DI, diagnosis  
diabetic retinopathy: TH, therapy  
disease exacerbation: DT, drug therapy  
female  
Gram negative infection: DT, drug therapy  
human  
infection control  
lung disease: DI, diagnosis  
lung disease: DT, drug therapy  
lung disease: ET, etiology  
lung disease: TH, therapy  
nephrotoxicity: SI, side effect  
orthostatic hypotension: SI, side effect  
prevalence  
survival time

CONTROLLED TERM: Drug Descriptors:

aminoglycoside: AE, adverse drug reaction  
aminoglycoside: CB, drug combination  
aminoglycoside: DT, drug therapy  
aminoglycoside: IV, intravenous drug administration  
amitriptyline: CB, drug combination  
beta lactam antibiotic: CB, drug combination  
beta lactam antibiotic: DT, drug therapy  
ceftazidime: DT, drug therapy  
diclofenac: AE, adverse drug reaction  
diclofenac: CB, drug combination  
insulin: DT, drug therapy  
lisinopril: AE, adverse drug reaction  
lisinopril: DT, drug therapy  
oral antidiabetic agent: DT, drug therapy  
oral antidiabetic agent: PO, oral drug administration  
tobramycin: DT, drug therapy

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (ceftazidime) 72558-82-8; (diclofenac) 15307-79-6, 15307-86-5; (insulin) 9004-10-8; (lisinopril) 76547-98-3, 83915-83-7; (tobramycin) 32986-56-4

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ACCESSION NUMBER: 2000065546 EMBASE Full-text

10/524815

TITLE: Breast disorders in the pediatric and adolescent patient.  
AUTHOR: Templeman, C.; Hertweck, S.P., Dr. (correspondence)  
CORPORATE SOURCE: Dept. of Obstetrics and Gynecology, University of  
Louisville, 550 S Jackson St, Louisville, KY 40292, United  
States.  
SOURCE: Obstetrics and Gynecology Clinics of North America, (2000)  
Vol. 27, No. 1, pp. 19-34.  
Refs: 78  
ISSN: 0889-8545 CODEN: OGCAE8  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review; (Review)  
FILE SEGMENT: 010 Obstetrics and Gynecology  
017 Public Health, Social Medicine and Epidemiology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
007 Pediatrics and Pediatric Surgery  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 2 Mar 2000  
Last Updated on STN: 2 Mar 2000

ABSTRACT: Despite the wide range of breast abnormalities that affect patients in the pediatric and adolescent populations, some conclusions can be drawn. Breast self-examination in the adolescent population is controversial but is recommended for girls who carry the BRCA1 or BRCA2 gene beginning at age 18 to 21 years. All girls with a disorder of breast size or symmetry should be given the opportunity of consultation with a plastic surgeon to discuss reconstructive options. Ultrasound is the most appropriate initial investigation in any adolescent patient with a breast mass owing to the dense nature of breast tissue in this age group. Although it is extremely rare in this population, breast cancer must always be included in the differential diagnosis of a breast mass, particularly in the patient with a prior history of childhood malignancy or chest irradiation.

CONTROLLED TERM: Medical Descriptors:  
\*adolescence  
adolescent  
\*breast cancer: DI, diagnosis  
\*breast cancer: EP, epidemiology  
\*breast cancer: ET, etiology  
\*breast cancer: PC, prevention  
breast development  
\*breast disease: CN, congenital disorder  
\*breast disease: DI, diagnosis  
\*breast disease: EP, epidemiology  
\*breast disease: ET, etiology  
\*breast disease: PC, prevention  
\*breast disease: SI, side effect  
breast examination  
breast hyperplasia: DI, diagnosis  
breast hyperplasia: ET, etiology  
breast hyperplasia: SU, surgery  
breast hypoplasia: DI, diagnosis  
breast hypoplasia: ET, etiology  
breast hypoplasia: SU, surgery  
\*breast malformation: CN, congenital disorder  
\*breast malformation: DI, diagnosis  
\*breast malformation: ET, etiology  
\*breast malformation: SU, surgery  
cystosarcoma phylloides: DI, diagnosis  
cystosarcoma phylloides: ET, etiology

cystosarcoma phylloides: SU, surgery  
 female  
 fibrocystic breast disease: DI, diagnosis  
 fibrocystic breast disease: DT, drug therapy  
 fibrocystic breast disease: ET, etiology  
 galactorrhea: SI, side effect  
 human  
 mastitis: DI, diagnosis  
 mastitis: DT, drug therapy  
 mastitis: ET, etiology  
 nipple malformation: CN, congenital disorder  
 nipple malformation: DI, diagnosis  
 nipple malformation: ET, etiology  
 patient counseling  
 Poland syndrome: CN, congenital disorder  
 Poland syndrome: DI, diagnosis  
 Poland syndrome: ET, etiology  
 priority journal  
 review

## CONTROLLED TERM:

Drug Descriptors:  
 amitriptyline: AE, adverse drug reaction  
 amphetamine: AE, adverse drug reaction  
 androgen: AE, adverse drug reaction  
 anesthetic agent: AE, adverse drug reaction  
 antibiotic agent: DT, drug therapy  
 chlorpromazine: AE, adverse drug reaction  
 cimetidine: AE, adverse drug reaction  
 domperidone: AE, adverse drug reaction  
 \*estrogen: AE, adverse drug reaction  
 \*estrogen: DT, drug therapy  
 \*estrogen: PO, oral drug administration  
 fluphenazine: AE, adverse drug reaction  
 haloperidol: AE, adverse drug reaction  
 \*medroxyprogesterone acetate: DT, drug therapy  
 \*medroxyprogesterone acetate: PO, oral drug administration  
 meprobamate: AE, adverse drug reaction  
 methyl dopa: AE, adverse drug reaction  
 methylxanthine  
 metoclopramide: AE, adverse drug reaction  
 monoamine oxidase inhibitor: AE, adverse drug reaction  
 narcotic agent: AE, adverse drug reaction  
 opiate: AE, adverse drug reaction  
 \*oral contraceptive agent: DT, drug therapy  
 \*oral contraceptive agent: PO, oral drug administration  
 primrose oil: DO, drug dose  
 primrose oil: DT, drug therapy  
 prostaglandin: AE, adverse drug reaction  
 reserpine: AE, adverse drug reaction  
 sulpiride: AE, adverse drug reaction  
 trifluoperazine: AE, adverse drug reaction

## CAS REGISTRY NO.:

(amitriptyline) 50-48-6, 549-18-8; (amphetamine)  
 1200-47-1, 139-10-6, 156-34-3, 2706-50-5, 300-62-9,  
 51-62-7, 60-13-9, 60-15-1; (chlorpromazine) 50-53-3,  
 69-09-0; (cimetidine) 51481-61-9, 70059-30-2; (domperidone)  
 57808-66-9; (fluphenazine) 146-56-5, 69-23-8; (haloperidol)  
 52-86-8; (medroxyprogesterone acetate) 71-58-9;  
 (meprobamate) 57-53-4; (methyl dopa) 555-29-3, 555-30-6;  
 (methylxanthine) 28109-92-4; (metoclopramide) 12707-59-4,  
 2576-84-3, 364-62-5, 7232-21-5; (opiate) 53663-61-9,  
 8002-76-4, 8008-60-4; (primrose oil) 65546-85-2;

(reserpine) 50-55-5, 8001-95-4; (sulpiride) 15676-16-1;  
(trifluoperazine) 117-89-5, 440-17-5

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ACCESSION NUMBER: 1999131082 EMBASE Full-text  
 TITLE: Adverse drug reactions in the urinary tract.  
 AUTHOR: Soomro, Naeem A. (correspondence)  
 CORPORATE SOURCE: Freeman Hospital, Newcastle upon Tyne NE7 7DN, United Kingdom.  
 AUTHOR: Neal, David E.  
 CORPORATE SOURCE: Medical School, University of Newcastle, Newcastle upon Tyne NE2 4HH, United Kingdom.  
 SOURCE: Adverse Drug Reaction Bulletin, (1998) No. 193, pp. 735-738.  
 Refs: 85  
 ISSN: 0044-6394 CODEN: ADRBBA  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; (Short Survey)  
 FILE SEGMENT: 028 Urology and Nephrology  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 29 Apr 1999  
 Last Updated on STN: 29 Apr 1999

ABSTRACT: Drugs can cause adverse effects on the urinary tract by a local action, or as a result of systemic effects on the autonomic nervous system, or central nervous control of bladder emptying. Tiaprofenic acid and cyclophosphamide as its metabolite acrolein, for example, can cause haemorrhagic cystitis. Localised retroperitoneal fibrosis, from methysergide, for instance, can lead to hydronephrosis. Agents with anticholinergic actions, such as the tricyclic antidepressants, can result in urinary retention, whilst alpha-adrenoceptor antagonists may lead to stress incontinence in females.

CONTROLLED TERM: Medical Descriptors:  
 autonomic nervous system  
 central nervous system  
 cystic fibrosis: DT, drug therapy  
 cystitis: SI, side effect  
 environmental exposure  
 hemorrhagic cystitis: DT, drug therapy  
 hemorrhagic cystitis: PC, prevention  
 hemorrhagic cystitis: SI, side effect  
 human  
 hydronephrosis: SI, side effect  
 inhalational drug administration  
 intravenous drug administration  
 micturition  
 oral drug administration  
 retroperitoneal fibrosis: SI, side effect  
 short survey  
 stress incontinence: SI, side effect  
 \*urinary tract disease: ET, etiology  
 \*urinary tract disease: SI, side effect  
 urine retention: SI, side effect  
 CONTROLLED TERM: Drug Descriptors:  
 acetylcysteine: DT, drug therapy

acrolein: AE, adverse drug reaction  
 allopurinol: AE, adverse drug reaction  
 alpha adrenergic receptor blocking agent: AE, adverse drug reaction  
 antibiotic agent: AE, adverse drug reaction  
 antineoplastic agent: AE, adverse drug reaction  
 busulfan: AE, adverse drug reaction  
 carbenicillin: AE, adverse drug reaction  
 carbenicillin: DT, drug therapy  
 carmustine: AE, adverse drug reaction  
 chlorambucil: AE, adverse drug reaction  
 chlormethine: AE, adverse drug reaction  
 cholinergic receptor blocking agent: AE, adverse drug reaction  
 cyclophosphamide: AE, adverse drug reaction  
 cyclophosphamide: PK, pharmacokinetics  
 danazol: AE, adverse drug reaction  
 drug metabolite: AE, adverse drug reaction  
 ether: AE, adverse drug reaction  
 isoniazid: AE, adverse drug reaction  
 mesna: AD, drug administration  
 mesna: DT, drug therapy  
 methenamine mandelate: AE, adverse drug reaction  
 methysergide: AE, adverse drug reaction  
 meticillin: AE, adverse drug reaction  
 nafcillin: AE, adverse drug reaction  
 penicillin g: AE, adverse drug reaction  
 piperacillin: AE, adverse drug reaction  
 piperacillin: DT, drug therapy  
 spasmolytic agent: AE, adverse drug reaction  
 tiaprofenic acid: AE, adverse drug reaction  
 ticarcillin: AE, adverse drug reaction  
 ticarcillin: DT, drug therapy  
 tricyclic antidepressant agent: AE, adverse drug reaction  
 unindexed drug: AE, adverse drug reaction  
 vincristine: AE, adverse drug reaction

CAS REGISTRY NO.: (acetylcysteine) 616-91-1; (acrolein) 107-02-8;  
 (allopurinol) 315-30-0; (busulfan) 55-98-1; (carbenicillin) 17230-86-3, 4697-36-3, 4800-94-6; (carmustine) 154-93-8;  
 (chlorambucil) 305-03-3; (chlormethine) 51-75-2, 55-86-7, 82905-71-3; (cyclophosphamide) 50-18-0; (danazol) 17230-88-5; (ether) 60-29-7; (isoniazid) 54-85-3, 62229-51-0, 65979-32-0; (mesna) 19767-45-4, 3375-50-6; (methenamine mandelate) 587-23-5; (methysergide) 16509-15-2, 361-37-5, 62288-72-6; (meticillin) 132-92-3, 38882-79-0, 61-32-5; (nafcillin) 147-52-4, 985-16-0; (penicillin G) 1406-05-9, 61-33-6; (piperacillin) 59703-84-3, 61477-96-1; (tiaprofenic acid) 33005-95-7; (ticarcillin) 29457-07-6, 34787-01-4, 4697-14-7; (vincristine) 57-22-7

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ACCESSION NUMBER: 1998246165 EMBASE Full-text  
 TITLE: Male breast disease.  
 AUTHOR: Gateley, C.A. (correspondence)  
 CORPORATE SOURCE: Royal Gwent Hospital, Newport NP9 2UB, United Kingdom.  
 SOURCE: Breast, (Jun 1998) Vol. 7, No. 3, pp. 121-127.  
 Refs: 45  
 ISSN: 0960-9776 CODEN: BREAEK

10/524815

COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review; (Review)  
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
016 Cancer  
037 Drug Literature Index  
038 Adverse Reactions Titles  
006 Internal Medicine

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 6 Aug 1998

Last Updated on STN: 6 Aug 1998

ABSTRACT: A variety of benign and malignant breast conditions affect the male breast. Gynaecomastia is common in puberty and old age and only when it is progressive or presents outwith these age groups are specific investigations indicated. Male breast cancer accounts for approximately 0.7% of all breast cancers. Lifetime risk for a male with an affected mother and sister is 2.3% and some of the families carry the BRCA2 gene. Infection is uncommon but when it does occur, causes include smoking in periareolar sepsis.

CONTROLLED TERM: Medical Descriptors:  
alcoholism: ET, etiology  
breast cancer: DT, drug therapy  
breast cancer: EP, epidemiology  
breast cancer: ET, etiology  
breast cancer: RT, radiotherapy  
breast cancer: SU, surgery  
\*breast disease: DT, drug therapy  
\*breast disease: EP, epidemiology  
\*breast disease: ET, etiology  
\*breast disease: RT, radiotherapy  
\*breast disease: SI, side effect  
\*breast disease: SU, surgery  
clinical examination  
drug effect  
fibrocystic breast disease: ET, etiology  
fibrocystic breast disease: TH, therapy  
gynecomastia: DT, drug therapy  
gynecomastia: ET, etiology  
gynecomastia: SI, side effect  
gynecomastia: SU, surgery  
human  
hyperthyroidism: ET, etiology  
infection: CO, complication  
infection: DT, drug therapy  
infection: SU, surgery  
kidney failure: ET, etiology  
klinefelter syndrome: CN, congenital disorder  
liver failure: ET, etiology  
male  
male breast  
mother  
nipple malformation: CO, complication  
priority journal  
puberty  
radiotherapy  
review  
senescence  
smoking  
starvation  
surgery



10/524815

testis disease: ET, etiology  
CONTROLLED TERM: Drug Descriptors:  
amiloride: AE, adverse drug reaction  
anabolic agent: AE, adverse drug reaction  
androgen: EC, endogenous compound  
antiandrogen: AE, adverse drug reaction  
antiinfective agent: AE, adverse drug reaction  
captopril: AE, adverse drug reaction  
clonidine: AE, adverse drug reaction  
danazol: DT, drug therapy  
domperidone: AE, adverse drug reaction  
estrogen: EC, endogenous compound  
ethionamide: AE, adverse drug reaction  
furosemide: AE, adverse drug reaction  
ibuprofen: AE, adverse drug reaction  
isoniazid: AE, adverse drug reaction  
methyldopa: AE, adverse drug reaction  
metoclopramide: AE, adverse drug reaction  
metronidazole: AE, adverse drug reaction  
nifedipine: AE, adverse drug reaction  
phenothiazine: AE, adverse drug reaction  
sex hormone: AE, adverse drug reaction  
tamoxifen: DT, drug therapy  
testosterone: AE, adverse drug reaction  
theophylline: AE, adverse drug reaction  
tricyclic antidepressant agent: AE, adverse drug reaction  
verapamil: AE, adverse drug reaction  
CAS REGISTRY NO.: (amiloride) 2016-88-8, 2609-46-3; (captopril) 62571-86-2;  
(clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (danazol)  
17230-88-5; (domperidone) 57808-66-9; (ethionamide)  
536-33-4; (furosemide) 54-31-9; (ibuprofen) 15687-27-1;  
(isoniazid) 54-85-3, 62229-51-0, 65979-32-0; (methyldopa)  
555-29-3, 555-30-6; (metoclopramide) 12707-59-4, 2576-84-3,  
364-62-5, 7232-21-5; (metronidazole) 39322-38-8, 443-48-1;  
(nifedipine) 21829-25-4; (phenothiazine) 92-84-2;  
(tamoxifen) 10540-29-1; (testosterone) 58-22-0;  
(theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1,  
99007-19-9; (verapamil) 152-11-4, 52-53-9  
  
L91 ANSWER 38 OF 49 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN  
ACCESSION NUMBER: 1997008554 EMBASE Full-text  
TITLE: The pathobiology of biliary epithelia.  
AUTHOR: Roberts, S.K.; Ludwig, J.; LaRusso, N.F., Dr.  
(correspondence)  
CORPORATE SOURCE: Basic Res. in Digestive Dis. Ctr., Mayo Medical School,  
Clinic and Foundation, 200 First Street Southwest,  
Rochester, MN 55905, United States.  
SOURCE: Gastroenterology, (1997) Vol. 112, No. 1, pp. 269-279.  
Refs: 63  
ISSN: 0016-5085 CODEN: GASTAB  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review; (Review)  
FILE SEGMENT: 037 Drug Literature Index  
038 Adverse Reactions Titles  
048 Gastroenterology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 28 Jan 1997  
Last Updated on STN: 28 Jan 1997

10/524815

ABSTRACT: Our understanding of the pathobiology of biliary epithelia is rapidly growing because of a surge of investigative activity. This became possible after suitable experimental models and techniques were developed with which to study cholangiocyte biology. Although the molecular mechanisms of bile formation by cholangiocytes and the role of these cells as a major cellular target in a variety of severe hepatobiliary diseases are currently being investigated, many questions remain unanswered, particularly regarding cholangiocellular functions, both in normal and abnormal conditions. As current experimental models become more refined, scientists with interests as diverse as cell biology and physiology, morphology, pharmacology, immunology, genetics, and oncology can be expected to further clarify the pathobiology of biliary epithelia.

CONTROLLED TERM: Medical Descriptors:  
acquired immune deficiency syndrome  
animal cell  
animal model  
bile duct carcinoma: ET, etiology  
\*bile duct disease: ET, etiology  
\*bile duct disease: SI, side effect  
biliary tract infection: ET, etiology  
cystic fibrosis: ET, etiology  
drug induced disease: ET, etiology  
drug induced disease: SI, side effect  
experimental model  
human  
human cell  
nonhuman  
pathophysiology  
primary sclerosing cholangitis: ET, etiology  
priority journal  
rat  
review

CONTROLLED TERM: Drug Descriptors:  
amitriptyline: AE, adverse drug reaction  
amoxicillin: AE, adverse drug reaction  
ampicillin: AE, adverse drug reaction  
carbamazepine: AE, adverse drug reaction  
chlorpromazine: AE, adverse drug reaction  
cromoglycate disodium: AE, adverse drug reaction  
cyproheptadine: AE, adverse drug reaction  
diazepam: AE, adverse drug reaction  
erythromycin: AE, adverse drug reaction  
haloperidol: AE, adverse drug reaction  
imipramine: AE, adverse drug reaction  
methyltestosterone: AE, adverse drug reaction  
paracetamol: AE, adverse drug reaction  
phenylbutazone: AE, adverse drug reaction  
prochlorperazine: AE, adverse drug reaction  
tiabendazole: AE, adverse drug reaction  
tolbutamide: AE, adverse drug reaction  
trifluoperazine: AE, adverse drug reaction  
troleandomycin: AE, adverse drug reaction

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (amoxicillin) 26787-78-0, 34642-77-8, 61336-70-7; (ampicillin) 69-52-3, 69-53-4, 7177-48-2, 74083-13-9, 94586-58-0; (carbamazepine) 298-46-4, 8047-84-5; (chlorpromazine) 50-53-3, 69-09-0; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (cyproheptadine) 129-03-3, 969-33-5; (diazepam) 439-14-5; (erythromycin) 114-07-8, 70536-18-4;

(haloperidol) 52-86-8; (imipramine) 113-52-0,  
~~50-49-7~~; (methyltestosterone) 58-18-4; (paracetamol)  
 103-90-2; (phenylbutazone) 129-18-0, 50-33-9, 8054-70-4;  
 (prochlorperazine) 58-38-8; (tiabendazole) 148-79-8;  
 (tolbutamide) 473-41-6, 64-77-7; (trifluoperazine)  
 117-89-5, 440-17-5; (troleandomycin) 2751-09-9

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ACCESSION NUMBER: 1998019436 EMBASE Full-text  
 TITLE: Obstetric issues in women with neurologic diseases.  
 AUTHOR: Norwitz, E.R., Dr. (correspondence); Repke, J.T.  
 CORPORATE SOURCE: Department of Obstetrics/Gynecology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States

SOURCE: Current Problems in Obstetrics, Gynecology and Fertility, (1997) Vol. 20, No. 6, pp. 190-230.

Refs: 279

ISSN: 8756-0410 CODEN: CPOIEN

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 010 Obstetrics and Gynecology  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 2 Feb 1998

Last Updated on STN: 2 Feb 1998

ABSTRACT: During pregnancy, the investigation and management of neurologic conditions is complicated by concern about the safety of the fetus. This manuscript is designed as a clinical reference for the practicing obstetrician. It will focus on the management of late pregnancy, labor, and delivery in patients with specific neurologic ailments. A systematic, anatomic approach has been taken. The review starts with a discussion of neurologic diseases of the brain and works its way down the spinal cord and peripheral nerves, across the neuromuscular junctions to the muscles. Movement disorders are considered separately. The monograph concludes with discussions of neurologic emergencies during pregnancy, as well as other situations specific to obstetric practice (such as drugs and breast-feeding, genetic counseling, and antenatal diagnosis for inherited neurologic diseases.) Disorders of the Brain includes discussions about the incidence, differential diagnosis, and management of a number of clinical conditions that center on the brain. These include headache; seizure disorders (focusing on management issues during pregnancy and implications for the fetus and newborn); cerebrovascular disease (stroke, Sheehan's syndrome, hypertensive encephalopathy); and demyelinating and degenerating diseases (multiple sclerosis, Huntington's disease). Infections of the nervous system (syphilis, polio, tetanus, toxoplasmosis, Lyme disease, HIV) occur in pregnancy, as they do in the nonpregnant state, but diagnosis and management might be different. The effects of inflammatory conditions of the central nervous system and intracranial tumors on pregnancy are reviewed briefly. There is a separate discussion about radiation exposure and its effects on the developing fetus. This discussion concludes that, in general, the use of radiographic technology (either diagnostic or therapeutic), if indicated, should not be restricted because the patient is pregnant. Psychiatric disorders affecting pregnancy (those that precede pregnancy, as well as conditions that result from pregnancy-such as postpartum depression and psychosis) often are overlooked. The warning signs and treatment of such conditions are discussed in detail. Disorders of the Spinal Cord includes discussions about specific topics (such as pregnancy in women with spinal-cord

injuries and the entity of autonomic dysreflexia), as well as some more general topics (such as backache in pregnancy). Disorders of Peripheral Nerves covers both mononeuropathies (carpal tunnel syndrome, Bell's palsy, meralgia paresthetica) and polyneuropathies (Guillain-Barre syndrome, porphyric neuropathy, and the hereditary polyneuropathies). The 'lithotomy' position derives its name from Greek 'lithos,' meaning stone, and 'otomy,' meaning to cut. It is so named because it was the position in which elderly men were placed for surgical removal of obstructing bladder stones. It is not a natural position for childbirth and might create nerve injury as the result of compression and/or stretching of a particular peripheral nerve or nerve plexus. Symptoms of such obstetric neuropathies are usually mild and unilateral, and complete recovery can be expected in the majority of cases. These are reviewed in greater detail. Disorders of the Neuromuscular Junction focuses on myasthenia gravis, its effect on pregnancy, implications for the fetus and newborn, and management during labor and delivery. Disorders of Muscle includes brief discussions about muscle cramping and a number of specific muscular disorders, such as myotonic dystrophy, myotonia congenita, and polymyositis/dermatomyositis. Movement disorders are considered separately. These include a definition of some of the generalized involuntary movements, with specific reference to chorea gravidarum and Wilson's disease. Localized involuntary movements are discussed briefly, including the 'restless leg syndrome,' which is reputed to be the most common movement disorder in pregnancy. It usually occurs in the third trimester and has been reported in up to 11% to 12% of all pregnancies. Neurologic Emergencies During Pregnancy reviews the management of such conditions as status epilepticus and disorders of consciousness (coma) during pregnancy and delivery. Miscellaneous Neurologic Conditions Specific to Pregnancy includes such topics as neurologic birth injury (intracranial hemorrhage, brachial-plexus injury, fetal acidosis, cerebral palsy) and other congenital neurologic injuries (facial nerve paralysis, injuries to the neck and spine, multicystic encephalomalacia). Many factors might put a fetus at risk for a genetic disorder or neurologic birth defect. The section Neurologic Disorders in the Fetus explores the need for comprehensive genetic counseling both before and after conception. A number of preventative measures are outlined. They might ameliorate the risk of congenital neurologic anomaly, such as meticulous periconceptional glucose control in women with insulin-dependent diabetes, folic acid supplementation for women who have had a previous fetus with neural-tube defect, and parental karyotyping for couples at risk of having a fetus with one of the more common autosomal recessive disorders (Tay-Sachs disease, cystic fibrosis, sickle cell anemia). Recommendations for routine prenatal screening (including maternal serum alpha-fetoprotein, triple-panel serum screening, ultrasonography, and amniocentesis and other fetal genetic testing) are reviewed in detail. The section ends with a detailed discussion on drugs and breast-feeding. In general, most chronic neurologic disorders are compatible with normal pregnancy outcome. Diagnostic investigations (including imaging studies) and treatment protocols should be initiated, if indicated. The implications of such interventions for the developing fetus, however, should not be overlooked.

CONTROLLED TERM:      Medical Descriptors:  
                          birth injury  
                          brain infection: DI, diagnosis  
                          brain tumor: DI, diagnosis  
                          cerebrovascular disease: DI, diagnosis  
                          coma  
                          degenerative disease: DI, diagnosis  
                          delivery  
                          demyelinating disease: DI, diagnosis  
                          diagnostic imaging  
                          differential diagnosis

epileptic state  
 female  
 fetus disease  
 genetic counseling  
 headache: DI, diagnosis  
 headache: DT, drug therapy  
 human  
 intravenous drug administration  
 labor  
 mental disease: DT, drug therapy  
 migraine: DI, diagnosis  
 migraine: DT, drug therapy  
 motor dysfunction: DI, diagnosis  
 myopathy: DI, diagnosis  
 \*neurologic disease  
 neuromuscular junction disorder: DI, diagnosis  
 \*obstetrics  
 peripheral neuropathy: DI, diagnosis  
 pregnancy  
 prenatal diagnosis  
 review  
 seizure: DI, diagnosis  
 seizure: DT, drug therapy  
 spinal cord disease: DI, diagnosis  
 Drug Descriptors:  
 amitriptyline: DT, drug therapy  
 \*anticonvulsive agent: DT, drug therapy  
 \*anticonvulsive agent: TO, drug toxicity  
 \*antimigraine agent: DT, drug therapy  
 anxiolytic agent: DT, drug therapy  
 carbamazepine: DT, drug therapy  
 carbamazepine: TO, drug toxicity  
 clomethiazole: DT, drug therapy  
 clomipramine: DT, drug therapy  
 clonazepam: DT, drug therapy  
 clonazepam: TO, drug toxicity  
 desipramine: DT, drug therapy  
 diazepam: DT, drug therapy  
 doxepin: DT, drug therapy  
 ethosuximide: DT, drug therapy  
 ethosuximide: TO, drug toxicity  
 felbamate: DT, drug therapy  
 felbamate: TO, drug toxicity  
 fluoxetine: DT, drug therapy  
 gabapentin: DT, drug therapy  
 gabapentin: TO, drug toxicity  
 imipramine: DT, drug therapy  
 klonopin  
 lamotrigine: DT, drug therapy  
 lamotrigine: TO, drug toxicity  
 magnesium sulfate: DT, drug therapy  
 monoamine oxidase inhibitor: DT, drug therapy  
 neuroleptic agent: DT, drug therapy  
 nortriptyline: DT, drug therapy  
 phenobarbital: DT, drug therapy  
 phenobarbital: TO, drug toxicity  
 phenytoin: DT, drug therapy  
 phenytoin: TO, drug toxicity  
 primidone: DT, drug therapy  
 primidone: TO, drug toxicity

CONTROLLED TERM:

\*psychotropic agent: DT, drug therapy  
 serotonin uptake inhibitor: DT, drug therapy  
 tricyclic antidepressant agent: DT, drug therapy  
 trimethadione: DT, drug therapy  
 trimethadione: TO, drug toxicity  
 unclassified drug  
 unindexed drug

valproic acid: DT, drug therapy  
 valproic acid: TO, drug toxicity  
 CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (carbamazepine)  
 298-46-4, 8047-84-5; (clomethiazole) 1867-58-9, 533-45-9;  
 (clomipramine) 17321-77-6, 303-49-1; (clonazepam)  
 1622-61-3; (desipramine) 50-47-5, 58-28-6; (diazepam)  
 439-14-5; (doxepin) 1229-29-4, 1668-19-5;  
 (ethosuximide) 77-67-8; (felbamate) 25451-15-4;  
 (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4;  
 (gabapentin) 60142-96-3; (imipramine) 113-52-0,  
 50-49-7; (lamotrigine) 84057-84-1; (magnesium sulfate)  
 7487-88-9; (nortriptyline) 72-69-5, 894-71-3;  
 (phenobarbital) 50-06-6, 57-30-7, 8028-68-0; (phenytoin)  
 57-41-0, 630-93-3; (primidone) 125-33-7; (trimethadione)  
 127-48-0; (valproic acid) 1069-66-5, 99-66-1  
 CHEMICAL NAME: adapin; anafranil; depakene; dilantin; elavil; felbatol;  
 klonipin; lamictal; luminal; mysoline; neurontin;  
 norpramin; pamelor; prozac; tegretol; tofranil; tridione;  
 zarontin

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ACCESSION NUMBER: 1996337659 EMBASE Full-text  
 TITLE: Use of a rapid HPLC assay for determination of  
 pharmacokinetic parameters of ibuprofen in patients with  
 cystic fibrosis.  
 AUTHOR: Rifai, Nader (correspondence); Sakamoto, Masayuki; Law,  
 Terence; Galpchian, Vartouhi; Harris, Neil  
 CORPORATE SOURCE: Department of Laboratory Medicine, Children's Hospital,  
 Harvard Medical School, Boston, MA, United States.  
 rifai@al.tch.harvard.edu  
 AUTHOR: Rifai, Nader (correspondence); Harris, Neil  
 CORPORATE SOURCE: Department of Pathology, Children's Hospital, Harvard  
 Medical School, Boston, MA, United States. rifai@al.tch.har  
 vard.edu  
 AUTHOR: Colin, Andrew A.  
 CORPORATE SOURCE: Department of Medicine, Children's Hospital, Harvard  
 Medical School, Boston, MA, United States.  
 AUTHOR: Rifai, Nader (correspondence)  
 CORPORATE SOURCE: Children's Hospital, Department of Laboratory Medicine, 300  
 Longwood Ave., Boston, MA 02115, United States. rifai@al.tc  
 h.harvard.edu  
 AUTHOR: Rifai, Nader (correspondence)  
 CORPORATE SOURCE: Department of Laboratory Medicine, Children's Hospital, 300  
 Longwood Ave., Boston, MA 02115, United States.  
 SOURCE: Clinical Chemistry, (1996) Vol. 42, No. 11, pp. 1812-1816.  
 Refs: 17  
 ISSN: 0009-9147 CODEN: CLCHAU  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English

10/524815

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 3 Dec 1996

Last Updated on STN: 3 Dec 1996

ABSTRACT: High doses of ibuprofen have been shown to delay the progression of lung disease without serious adverse effects in patients with cystic fibrosis. To be effective, peak ibuprofen concentration of 50 to 100 mg/L has to be achieved. We developed an HPLC assay to rapidly determine plasma ibuprofen concentration. We used this assay to determine the pharmacokinetics of ibuprofen in patients with cystic fibrosis. The assay possessed linearity up to 500 mg/L, sensitivity to 1 mg/L, average recovery of 98%, and run-to-run precision (n = 23) of 3%. Furthermore, the assay proved to be free of interference from 51 medications. Observed time to peak concentration varied significantly between those receiving ibuprofen tablets (mean + SD, 94 ± 29 min, n = 16) and syrup (30 ± 0 min, n = 4) (P < 0.0001). We conclude that the method described here is ideal for therapeutic monitoring of ibuprofen.

CONTROLLED TERM: Medical Descriptors:

adolescent

adult

article

child

clinical article

clinical trial

\*cystic fibrosis: CN, congenital disorder

disease course

drug absorption

drug blood level

drug determination

drug formulation

drug half life

drug monitoring

female

human

\*inflammation

male

oral drug administration

reversed phase high performance liquid chromatography

CONTROLLED TERM: Drug Descriptors:

acecainide

acetylsalicylic acid

amikacin

amitriptyline

\*antiarrhythmic agent

antibiotic agent

\*anticonvulsive agent

\*antidepressant agent

\*antiinflammatory agent

brompheniramine

caffeine

cefazolin

clonazepam

clotrimazole

digitoxin

digoxin

disopyramide

doxepin

felbamate

ibufenac

\*ibuprofen: CT, clinical trial

\*ibuprofen: AD, drug administration  
 \*ibuprofen: AN, drug analysis  
 \*ibuprofen: CR, drug concentration  
 \*ibuprofen: PR, pharmaceuticals  
 \*ibuprofen: PK, pharmacokinetics  
 imipenem  
 ketoprofen  
 lidocaine  
 metharbital  
 paracetamol  
 phenytoin  
 \*propionic acid derivative  
 tobramycin  
 unindexed drug

CAS REGISTRY NO.: (acecainide) 32795-44-1, 34118-92-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (amikacin) 37517-28-5, 39831-55-5; (~~amitriptyline~~) ~~50-48-6~~, ~~549-18-8~~; (brompheniramine) 86-22-6, 980-71-2; (caffeine) 30388-07-9, 58-08-2; (cefazolin) 25953-19-9, 27164-46-1; (clonazepam) 1622-61-3; (clotrimazole) 23593-75-1; (digitoxin) 71-63-6; (digoxin) 20830-75-5, 57285-89-9; (disopyramide) 3737-09-5; (~~doxepin~~) 1229-29-4, ~~1668-19-5~~; (felbamate) 25451-15-4; (ibufenac) 1553-60-2; (ibuprofen) 15687-27-1; (imipenem) 64221-86-9; (ketoprofen) 22071-15-4, 57495-14-4; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (metharbital) 50-11-3; (paracetamol) 103-90-2; (phenytoin) 57-41-0, 630-93-3; (tobramycin) 32986-56-4

CHEMICAL NAME: (1) motrin

COMPANY NAME: (1) upjohn (United States); sigma (United States)

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ACCESSION NUMBER: 1996212929 EMBASE Full-text  
 TITLE: Obstructive lung disease and sleep.  
 AUTHOR: Jokic, R.; Fitzpatrick, M.F., Dr. (correspondence)  
 CORPORATE SOURCE: Department of Medicine, University of Saskatchewan, Royal University Hospital, Saskatoon, Sask. S7N 0X0, Canada.  
 SOURCE: Medical Clinics of North America, (1996) Vol. 80, No. 4, pp. 821-850.  
 ISSN: 0025-7125 CODEN: MCNAA9  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 037 Drug Literature Index  
 006 Internal Medicine  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 14 Aug 1996  
 Last Updated on STN: 14 Aug 1996

ABSTRACT: There is a significant interaction between obstructive lung disease and sleep-sleep is associated with clinical deterioration in obstructive lung disease, and vice versa. Knowledge of the pathophysiology of deterioration in obstructive lung disease during sleep is essential to the understanding of the management of this problem. Recent information has helped clarify this pathophysiology and has led to more aggressive treatment for deterioration of obstructive lung disease during sleep. Whether this newer and more aggressive treatment strategy improves survival or morbidity in these conditions is a challenge for future research.



10/524815

CONTROLLED TERM: Medical Descriptors:  
alcohol consumption  
breathing pattern  
\*chronic obstructive lung disease: DT, drug therapy  
\*chronic obstructive lung disease: TH, therapy  
\*cystic fibrosis: TH, therapy  
functional residual capacity  
human  
\*hypoxemia: CO, complication  
oxygen therapy  
positive end expiratory pressure  
priority journal  
review  
\*sleep  
\*sleep apnea syndrome: DT, drug therapy  
\*sleep apnea syndrome: TH, therapy

CONTROLLED TERM: Drug Descriptors:  
\*acetazolamide: DT, drug therapy  
\*almitrine: DO, drug dose  
\*almitrine: DT, drug therapy  
\*gestagen: DT, drug therapy  
\*hypnotic sedative agent: DT, drug therapy  
\*protriptyline: DT, drug therapy  
\*theophylline: DT, drug therapy

CAS REGISTRY NO.: (acetazolamide) 1424-27-7, 59-66-5; (almitrine) 27469-53-0;  
(protriptyline) 1225-55-4, 438-60-8; (theophylline)  
58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9

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ACCESSION NUMBER: 1996321652 EMBASE Full-text  
TITLE: Chronic pain in cystic fibrosis.  
AUTHOR: Ravilly, S.; Robinson, W.; Suresh, S.; Wohl, M.E.; Berde, C.B., Dr. (correspondence)  
CORPORATE SOURCE: Pain Treatment Service, Department of Anesthesia, Children's Hospital, 300 Longwood Ave, Boston, MA 02115, United States.  
SOURCE: Pediatrics, (1996) Vol. 98, No. 4, pp. 741-747.  
ISSN: 0031-4005 CODEN: PEDIAU  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 024 Anesthesiology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
006 Internal Medicine  
007 Pediatrics and Pediatric Surgery  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 12 Nov 1996  
Last Updated on STN: 12 Nov 1996

ABSTRACT: Objective. The objective of this study was to examine the incidence and therapy of chronic pain in a group of older patients with cystic fibrosis (CF). Patients. We identified two groups of patients followed at the CF Center at Children's Hospital (Boston); the first group consisted of all patients above the age of 5 years who died between 1984 and 1993, and the second was a cohort of 23 additional CF patients who had been referred to the Pain Treatment Service. Design. Medical charts were reviewed for the etiology and therapy of all pain episodes requiring medical intervention. Results. The incidence of chronic pain in this population increased sharply in the last 6 months of life. Headaches (55% of patients) and chest pain (65%) were

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frequently reported, although back pain (19%), abdominal pain (19%), and limb pain (16%) were also reported. In patients with headache, the main etiologies were hypercarbia or hypoxia, migraine, and sinusitis. The majority of chest pain was musculoskeletal, with pleuritis, pneumothorax, and rib fracture also reported as the cause of chest pain. Interventions. A variety of nonpharmacological and pharmacological therapies were reported. Forty-one patients (53%) had pain severe enough to require opioid treatment, and 10 patients (13%) received opioids for more than 3 months. In eight patients with more severe pain, regional analgesia was found to be particularly effective. Conclusions. Chronic pain is a common problem in CF, particularly as the patient population ages. When administered with caution, opioids have proven to be effective and safe in this population; regional anesthesia can be used to preserve pulmonary toilet while adequately treating severe pain.

CONTROLLED TERM: Medical Descriptors:  
abdominal pain  
acupuncture  
adolescent  
adult  
article  
backache  
bleeding: SI, side effect  
\*chronic pain: DT, drug therapy  
\*chronic pain: TH, therapy  
\*cystic fibrosis: CN, congenital disorder  
female  
headache  
human  
hypercapnia  
hypoxia  
major clinical study  
male  
migraine  
nerve stimulation  
pleurisy  
pneumothorax  
priority journal  
rib fracture  
school child  
sinusitis  
thorax epidural anesthesia  
thorax pain

CONTROLLED TERM: Drug Descriptors:  
ketorolac: DT, drug therapy  
\*morphine: DT, drug therapy  
\*nonsteroid antiinflammatory agent: AE, adverse drug reaction  
\*nonsteroid antiinflammatory agent: DT, drug therapy  
\*opiate: DT, drug therapy  
salazosulfapyridine: DT, drug therapy  
sumatriptan: DT, drug therapy  
trazodone: DT, drug therapy  
tricyclic antidepressant agent: DT, drug therapy

CAS REGISTRY NO.: (ketorolac) 74103-06-3; (morphine) 52-26-6, 57-27-2;  
(opiate) 53663-61-9, 8002-76-4, 8008-60-4;  
(salazosulfapyridine) 599-79-1; (sumatriptan) 103628-46-2;  
(trazodone) 19794-93-5, 25332-39-2

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ACCESSION NUMBER: 1996011372 EMBASE Full-text  
TITLE: Persistent visceral pain in adolescents.  
AUTHOR: Zeltzer, Lonnie, Dr. (correspondence); Koh, Jeffrey;  
Hamilton, Alison  
CORPORATE SOURCE: Depts. of Pediat. and Anesthesiology, Harbor-UCLA Medical  
Center, University of California, Los Angeles, CA, United  
States.  
AUTHOR: Hyman, Paul  
CORPORATE SOURCE: Department of Pediatrics, Harbor-UCLA Medical Center,  
University of California, Los Angeles, CA, United States.  
AUTHOR: Heyman, Melvin  
CORPORATE SOURCE: Division of Gastroenterology, Department of Pediatrics,  
Univ. of California at San Francisco, San Francisco, CA,  
United States.  
AUTHOR: Boyce, W. Thomas  
CORPORATE SOURCE: Division of Behavioral Pediatrics, Department of  
Pediatrics, Univ. of California at San Francisco, San  
Francisco, CA, United States.  
AUTHOR: Zwass, Maurice  
CORPORATE SOURCE: Department of Anesthesiology, Univ. of California at San  
Francisco, San Francisco, CA, United States.  
AUTHOR: Feldman, Edward J.  
CORPORATE SOURCE: Department of Medicine, Cedars-Sinai Medical Center, Univ.  
of California at Los Angeles, Los Angeles, CA, United  
States.  
AUTHOR: Zeltzer, Lonnie, Dr. (correspondence)  
CORPORATE SOURCE: Department of Pediatrics, UCLA School of Medicine, 22-464  
MDCC, 10833 LeConte Ave., Los Angeles, CA 90024-1752,  
United States.  
SOURCE: Journal of Pediatric Gastroenterology and Nutrition, (1996)  
Vol. 22, No. 1, pp. 92-98.  
Refs: 10  
ISSN: 0277-2116 CODEN: JPGND6  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 037 Drug Literature Index  
048 Gastroenterology  
007 Pediatrics and Pediatric Surgery  
LANGUAGE: English  
ENTRY DATE: Entered STN: 30 Jan 1996  
Last Updated on STN: 30 Jan 1996  
CONTROLLED TERM: Medical Descriptors:  
adolescent  
anorexia  
article  
case report  
colon resection  
cystic fibrosis: CN, congenital disorder  
diarrhea  
dose response  
\*enteritis: DT, drug therapy  
\*enteritis: SU, surgery  
\*hiccup  
human  
human tissue  
hypnosis  
male  
nausea: DT, drug therapy  
priority journal  
\*visceral pain: DT, drug therapy

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CONTROLLED TERM: \*visceral pain: TH, therapy  
Drug Descriptors:  
amitriptyline  
\*bupivacaine: DO, drug dose  
\*bupivacaine: DT, drug therapy  
carbamazepine  
cisapride  
clonidine  
desipramine  
erythromycin  
ibuprofen  
\*lidocaine: DT, drug therapy  
lorazepam  
\*opiate: DT, drug therapy  
prednisone: DO, drug dose  
prednisone: DT, drug therapy  
promethazine: DT, drug therapy  
ranitidine  
CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (bupivacaine)  
18010-40-7, 2180-92-9, 55750-21-5; (carbamazepine)  
298-46-4, 8047-84-5; (cisapride) 81098-60-4; (clonidine)  
4205-90-7, 4205-91-8, 57066-25-8; (desipramine)  
50-47-5, 58-28-6; (erythromycin) 114-07-8, 70536-18-4;  
(ibuprofen) 15687-27-1; (lidocaine) 137-58-6, 24847-67-4,  
56934-02-2, 73-78-9; (lorazepam) 846-49-1; (opiate)  
53663-61-9, 8002-76-4, 8008-60-4; (prednisone) 53-03-2;  
(promethazine) 58-33-3, 60-87-7; (ranitidine) 66357-35-5,  
66357-59-3  
CHEMICAL NAME: ativan; tegretol

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ACCESSION NUMBER: 1996009696 EMBASE Full-text  
TITLE: Iontophoresis for enhancing penetration of dermatologic and antiviral drugs.  
AUTHOR: Gangarosa Sr., L.P. (correspondence); Ozawa, A.; Ohkido, M.; Shimomura, Y.; Hill, J.M.  
CORPORATE SOURCE: Dept. of Oral Biology-Pharmacology, School of Dentistry, Medical College of Georgia, Augusta, GA 30912-1128, United States.  
SOURCE: Journal of Dermatology, (1995) Vol. 22, No. 11, pp. 865-875.  
ISSN: 0385-2407 CODEN: JDMYAG  
COUNTRY: Japan  
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)  
FILE SEGMENT: 013 Dermatology and Venereology  
024 Anesthesiology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 30 Jan 1996  
Last Updated on STN: 30 Jan 1996

ABSTRACT: Iontophoresis is the process of introducing ionic drugs into the body for therapeutic purposes. Although iontophoresis has the potential for systemic therapy, it has mainly been used for local therapy at body surfaces. Many ionic drugs are available including lidocaine, epinephrine, methylprednisolone succinate, dexamethasone phosphate, several antivirals, various antibiotics, and other specific drugs. The use of an indicated ionic drug by iontophoresis offers a broad potential for promoting the development of more effective therapies in dermatology. Iontophoresis of ionized drugs

provided a 20-60 fold increase in penetration over topical application. Iontophoresis for dermatological use requires that: a) a charged drug be placed at an electrode having a polarity the same charge as the drug, b) the condition or disease under treatment be at or near the body surface, and c) a modern, sophisticated source of direct current, with appropriate accessories, be used. The current source must have features that make it not only effective, but also safe for application to the patient. Modern systems for application of drugs by iontophoresis have features that make the process simple and efficient for use in practice. Iontophoresis has a long history of use, having been suggested for various therapies for many years in medicine, physical therapy and dentistry. Pilocarpine iontophoresis is a preferred method for ~~cystic~~ fibrosis detection. Also, lidocaine iontophoresis has been advocated to anesthetize the tympanic membrane before myringotomy. Anesthesia of the skin to a depth of 1.0 cm or more has been reported in double-blind studies of human volunteers. Local anesthesia by iontophoresis was reported to be effective for: 1) cutaneous cutdowns in patients requiring kidney dialysis, 2) delicate eyelid surgery, as the sole anesthetic, 3) preinjection topical anesthesia, and 4) shave biopsies of skin lesions. The use of iontophoresis for treating difficult cases of hyperhidrosis is quite popular among dermatologists. The present report emphasizes uses of iontophoresis in dermatology and is divided into discussion of studies using iontophoresis for postherpetic neuralgia, local anesthesia, antiviral therapy, and for corticosteroid therapy of nonspecific inflammatory lesions. Over 1250 patients have been treated for postherpetic neuralgia by corticosteroid iontophoresis at 6 medical centers with 60-80% of patients showing a major therapeutic response with return to a tolerable pain level. Double-blind studies of varicella zoster (active and postherpetic) and herpes simplex have proven that iontophoresis is a valuable modality for treating vital diseases of the skin. Many other uses for iontophoresis have been proposed in the literature that involves several hundred research papers, several textbooks and many book chapters. Review of the literature supports the concept that iontophoresis provides an optimal method for drug application in therapy of surface tissues.

CONTROLLED TERM: Medical Descriptors:  
 burn: CO, complication  
 clinical trial  
 conference paper  
 corticosteroid therapy  
 drug penetration  
 herpes labialis: DT, drug therapy  
 \*herpes simplex: DI, diagnosis  
 \*herpes simplex: DT, drug therapy  
 \*herpes zoster: DI, diagnosis  
 \*herpes zoster: DT, drug therapy  
 human  
 intravenous drug administration  
 \*iontophoresis  
 local anesthesia  
 nonhuman  
 oral drug administration  
 \*postherpetic neuralgia: DI, diagnosis  
 \*postherpetic neuralgia: DT, drug therapy  
 topical drug administration

CONTROLLED TERM: Drug Descriptors:  
 aciclovir: AD, drug administration  
 aciclovir: DT, drug therapy  
 aciclovir: PR, pharmaceuticals  
 amitriptyline: CB, drug combination  
 amitriptyline: DT, drug therapy  
 antidepressant agent: CB, drug combination

antidepressant agent: DT, drug therapy  
 \*antivirus agent: AD, drug administration  
 \*antivirus agent: DT, drug therapy  
 \*antivirus agent: PR, pharmaceuticals  
 carbamazepine: AD, drug administration  
 carbamazepine: DT, drug therapy  
 carbamazepine: PR, pharmaceuticals  
 \*corticosteroid: AD, drug administration  
 \*corticosteroid: DT, drug therapy  
 \*corticosteroid: PR, pharmaceuticals  
 idoxuridine: AD, drug administration  
 idoxuridine: DT, drug therapy  
 idoxuridine: PR, pharmaceuticals  
 lidocaine: AD, drug administration  
 lidocaine: DT, drug therapy  
 lidocaine: PR, pharmaceuticals  
 methylprednisolone sodium succinate: AD, drug administration  
 methylprednisolone sodium succinate: DT, drug therapy  
 methylprednisolone sodium succinate: PR, pharmaceuticals  
 naproxen: AD, drug administration  
 naproxen: CB, drug combination  
 naproxen: DT, drug therapy  
 naproxen: PR, pharmaceuticals  
 nonsteroid antiinflammatory agent: AD, drug administration  
 nonsteroid antiinflammatory agent: CB, drug combination  
 nonsteroid antiinflammatory agent: DT, drug therapy  
 nonsteroid antiinflammatory agent: PR, pharmaceuticals  
 sodium nitrate: AD, drug administration  
 sodium nitrate: DT, drug therapy  
 sodium nitrate: PR, pharmaceuticals  
 triflupromazine: CB, drug combination  
 triflupromazine: DT, drug therapy  
 vidarabine: AD, drug administration  
 vidarabine: DT, drug therapy  
 vidarabine: PR, pharmaceuticals  
 vidarabine phosphate: AD, drug administration  
 vidarabine phosphate: DT, drug therapy  
 vidarabine phosphate: PR, pharmaceuticals

CAS REGISTRY NO.: (aciclovir) 59277-89-3; (~~amitriptyline~~) 50-48-6, 549-18-8; (carbamazepine) 298-46-4, 8047-84-5; (idoxuridine) 54-42-2; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (methylprednisolone sodium succinate) 2375-03-3, 2921-57-5; (naproxen) 22204-53-1, 26159-34-2; (sodium nitrate) 7631-99-4; (triflupromazine) 1098-60-8, 146-54-3; (vidarabine phosphate) 29984-33-6; (vidarabine) 2006-02-2, 5536-17-4

CHEMICAL NAME: anaprox; ~~elavil~~; naproxyn; solumedrol; tegretol

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ACCESSION NUMBER: 1996098410 EMBASE Full-text  
 TITLE: What's new in pediatric dermatology.  
 AUTHOR: Bonifazi, E.  
 SOURCE: European Journal of Pediatric Dermatology, (1995) Vol. 5, No. 2, pp. 81-85.  
 ISSN: 1122-7672 CODEN: EPDDE9  
 COUNTRY: Italy  
 DOCUMENT TYPE: Journal; (Short Survey)  
 FILE SEGMENT: 013 Dermatology and Venereology

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037 Drug Literature Index  
007 Pediatrics and Pediatric Surgery

LANGUAGE: English  
ENTRY DATE: Entered STN: 30 Apr 1996  
Last Updated on STN: 30 Apr 1996

CONTROLLED TERM: Medical Descriptors:  
child  
\*cystic fibrosis  
human  
intramuscular drug administration  
intravenous drug administration  
oral drug administration  
\*pruritus: DT, drug therapy  
short survey  
\*skin disease: CO, complication  
\*skin disease: DI, diagnosis  
\*skin disease: DT, drug therapy  
\*skin disease: ET, etiology  
topical drug administration

CONTROLLED TERM: Drug Descriptors:  
alpha tocopherol: DT, drug therapy  
alprazolam: DT, drug therapy  
amitriptyline: DT, drug therapy  
antibiotic agent: DT, drug therapy  
buspirone: DT, drug therapy  
cimetidine: DT, drug therapy  
clomipramine: DT, drug therapy  
cyclosporin: DT, drug therapy  
dicloxacillin: DT, drug therapy  
diphenhydramine: DT, drug therapy  
doxepin: DT, drug therapy  
fluconazole: DT, drug therapy  
fluoxetine: DT, drug therapy  
haloperidol: DT, drug therapy  
hydroxyzine: DT, drug therapy  
immunoglobulin: DT, drug therapy  
isotretinoin: DT, drug therapy  
ivermectin: DT, drug therapy  
nortriptyline: DT, drug therapy  
penicillin g: DT, drug therapy  
pimozide: DT, drug therapy  
prednisone: DT, drug therapy  
procaine penicillin: DT, drug therapy  
procaine plus lidocaine: DT, drug therapy  
pseudomonic acid: DT, drug therapy  
psychotropic agent: DT, drug therapy  
sertraline: DT, drug therapy  
tetracycline: DT, drug therapy  
unclassified drug

CAS REGISTRY NO.: (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4,  
58-95-7, 59-02-9; (alprazolam) 28981-97-7;  
(amitriptyline) ~~50-48-6~~, 549-18-8; (buspirone)  
33386-08-2, 36505-84-7; (cimetidine) 51481-61-9,  
70059-30-2; (clomipramine) 17321-77-6, 303-49-1;  
(cyclosporin) 79217-60-0; (dicloxacillin) 13412-64-1,  
3116-76-5, 343-55-5; (diphenhydramine) 147-24-0, 58-73-1;  
(doxepin) 1229-29-4, ~~1668-19-5~~; (fluconazole)  
86386-73-4; (fluoxetine) 54910-89-3, 56296-78-7,  
59333-67-4; (haloperidol) 52-86-8; (hydroxyzine) 2192-20-3,  
64095-02-9, 68-88-2; (immunoglobulin) 9007-83-4;

(isotretinoin) 4759-48-2; (ivermectin) 70288-86-7;  
 (nortriptyline) 72-69-5, 894-71-3; (penicillin G)  
 1406-05-9, 61-33-6; (pimozide) 2062-78-4; (prednisone)  
 53-03-2; (procaine penicillin) 54-35-3, 6130-64-9;  
 (pseudomonic acid) 12650-69-0, 40980-51-6, 71980-98-8;  
 (sertraline) 79617-96-2; (tetracycline) 23843-90-5,  
 60-54-8, 64-75-5

CHEMICAL NAME: anafranil; atarax; benadryl; buspar; ~~elavil~~; haldol;  
 orap; pamelor; prozac; sinequan; xanax; zoloft

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ACCESSION NUMBER: 1994279719 EMBASE Full-text  
 TITLE: Benign tumors of the breast.  
 AUTHOR: Isaacs, J.H., Dr. (correspondence)  
 CORPORATE SOURCE: Department of Obstetrics/Gynecology, Loyola University,  
 3008 Indian Wood Road, Wilmette, IL 60091-1130, United States.  
 SOURCE: Obstetrics and Gynecology Clinics of North America, (1994)  
 Vol. 21, No. 3, pp. 487-497.  
 ISSN: 0889-8545 CODEN: OGCAE8  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 010 Obstetrics and Gynecology  
 003 Endocrinology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 005 General Pathology and Pathological Anatomy  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

ABSTRACT: Most patients who consult their physician for 'breast lesions' do not have a malignancy of the breast. The benign lesions of the breast include fibrocystic condition, macrocyst fibroadenomas, and intraductal papillomas. Nipple discharge is a common condition, and the diagnosis and treatment is discussed. Rarer benign tumors such as adenoid tumors, lipomas, neurofibromatosis, benign fibrous histiocytooma, and glandular cell tumors are briefly discussed.

CONTROLLED TERM: Medical Descriptors:  
 breast abscess: SU, surgery  
 breast biopsy  
 breast cancer: DI, diagnosis  
 \*breast cyst: DI, diagnosis  
 breast discharge: DI, diagnosis  
 breast duct ectasia: DI, diagnosis  
 breast duct ectasia: ET, etiology  
 breast milk: EC, endogenous compound  
 breast papilloma: DI, diagnosis  
 breast papilloma: SU, surgery  
 \*breast tumor: DI, diagnosis  
 \*breast tumor: DT, drug therapy  
 \*breast tumor: ET, etiology  
 \*breast tumor: SU, surgery  
 estrogen therapy  
 female  
 \*fibroadenoma: DI, diagnosis  
 \*fibroadenoma: SU, surgery  
 \*fibrocystic breast disease: DI, diagnosis  
 galactorrhea: CO, complication  
 galactorrhea: DI, diagnosis



galactorrhea: DT, drug therapy  
 galactorrhea: ET, etiology  
 galactorrhea: SI, side effect  
 human  
 mammography  
 mastalgia: CO, complication  
 mastalgia: DT, drug therapy  
 mastalgia: ET, etiology  
 mastitis: DT, drug therapy  
 physical examination  
 priority journal  
 review  
 Tietze syndrome: CO, complication  
 Tietze syndrome: DI, diagnosis  
 Tietze syndrome: DT, drug therapy

## CONTROLLED TERM:

Drug Descriptors:  
 antibiotic agent: DT, drug therapy  
 antiinflammatory agent: DT, drug therapy  
 bromocriptine mesilate: DO, drug dose  
 bromocriptine mesilate: DT, drug therapy  
 bromocriptine mesilate: PD, pharmacology  
 estrogen: DT, drug therapy  
 estrogen: EC, endogenous compound  
 hexachlorophene  
 ice  
 lactose: EC, endogenous compound  
 methyl dopa: AE, adverse drug reaction  
 nonsteroid antiinflammatory agent: DT, drug therapy  
 oral contraceptive agent: AE, adverse drug reaction  
 oral contraceptive agent: AD, drug administration  
 phenothiazine derivative: AE, adverse drug reaction  
 povidone iodine  
 progesterone: DT, drug therapy  
 prolactin: EC, endogenous compound  
 Rauwolfia alkaloid: AE, adverse drug reaction  
 tricyclic antidepressant agent: AE, adverse drug reaction

## CAS REGISTRY NO.:

(bromocriptine mesilate) 22260-51-1; (hexachlorophene)  
 11119-93-0, 70-30-4; (lactose) 10039-26-6, 16984-38-6,  
 63-42-3, 64044-51-5; (methyl dopa) 555-29-3, 555-30-6;  
 (povidone iodine) 25655-41-8; (progesterone) 57-83-0;  
 (prolactin) 12585-34-1, 50647-00-2, 9002-62-4

## CHEMICAL NAME:

parlodel

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ACCESSION NUMBER: 1992160861 EMBASE Full-text

TITLE: Bayesian parameter estimation and population pharmacokinetics.

AUTHOR: Thomson, A.H., Dr. (correspondence); Whiting, B.

CORPORATE SOURCE: Dept of Medicine and Therapeutics, Western Infirmary, Glasgow G11 6NT, United Kingdom.

SOURCE: Clinical Pharmacokinetics, (1992) Vol. 22, No. 6, pp. 447-467.

ISSN: 0312-5963 CODEN: CPKNDH

COUNTRY: New Zealand

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

10/524815

ENTRY DATE: Entered STN: 21 Jun 1992

Last Updated on STN: 21 Jun 1992

ABSTRACT: The widespread application of Bayesian parameter estimation in the area of therapeutic drug monitoring (TDM) has prompted the need for well conducted population studies to obtain relevant prior pharmacokinetic parameter estimates. In many cases the population has consisted of a relatively small number of subjects. This may be unavoidable for drugs used in cancer chemotherapy or in small, specific populations of patients. In contrast, information about drugs which are used extensively, such as the aminoglycosides, can be obtained by population studies which involve a large number of individuals. Indeed, this technique has proved particularly useful for determining parameter estimates which can be employed in neonatal TDM. Bayesian parameter estimation has been most frequently used for drugs with narrow therapeutic ranges such as the aminoglycosides, cyclosporin, digoxin, anticonvulsants (especially phenytoin), lithium and theophylline. However, the technique has now been extended to cytotoxic drugs, Factor VIII and warfarin. Bayesian methods have also been used to limit the number of samples required in more conventional pharmacokinetic studies with new drugs. Further advances in the use of these methods are likely to include measures of drug response and toxicity requiring population studies which also include relevant pharmacodynamic information.

CONTROLLED TERM: Medical Descriptors:

- \*bayes theorem
- cancer chemotherapy
- cystic fibrosis
- drug blood level
- drug monitoring
- drug response
- drug urine level
- forecasting
- neonatology
- \*pharmacokinetics
- \*population research
- priority journal
- review
- sample
- toxicity

CONTROLLED TERM: Drug Descriptors:

- alfentanil: PK, pharmacokinetics
- aminoglycoside: PK, pharmacokinetics
- anticonvulsive agent: PK, pharmacokinetics
- bentazepam: PK, pharmacokinetics
- blood clotting factor 8: PK, pharmacokinetics
- ceftazidime: PK, pharmacokinetics
- ciprofloxacin: PK, pharmacokinetics
- cyclosporin: PK, pharmacokinetics
- cytotoxic agent: PK, pharmacokinetics
- digoxin: PK, pharmacokinetics
- heparin: PK, pharmacokinetics
- imipramine: PK, pharmacokinetics
- lidocaine: PK, pharmacokinetics
- lithium: PK, pharmacokinetics
- midazolam: PK, pharmacokinetics
- piperacillin: PK, pharmacokinetics
- theophylline: PK, pharmacokinetics
- vancomycin: PK, pharmacokinetics
- warfarin: PK, pharmacokinetics

CAS REGISTRY NO.: (alfentanil) 69049-06-5, 71195-58-9; (bentazepam) 29462-18-8; (blood clotting factor 8) 9001-27-8;

(ceftazidime) 72558-82-8; (ciprofloxacin) 85721-33-1;  
 (cyclosporin) 79217-60-0; (digoxin) 20830-75-5, 57285-89-9;  
 (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5;  
 (imipramine) 113-52-0, 50-49-7; (lidocaine) 137-58-6,  
 24847-67-4, 56934-02-2, 73-78-9; (lithium) 7439-93-2;  
 (midazolam) 59467-70-8; (piperacillin) 59703-84-3,  
 61477-96-1; (theophylline) 58-55-9, 5967-84-0, 8055-07-0,  
 8061-56-1, 99007-19-9; (vancomycin) 1404-90-6, 1404-93-9;  
 (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8,  
 81-81-2

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ACCESSION NUMBER: 1991065459 EMBASE Full-text  
 TITLE: Chronic bronchial secretion in  $\Delta$ F508 heterozygote for cystic fibrosis.  
 AUTHOR: Smith, D.L.; Stableforth, D.E.; Cushley, M.  
 CORPORATE SOURCE: Adult Cystic Fibrosis Unit, East Birmingham Hospital, Birmingham B9 5ST, United Kingdom.  
 SOURCE: Lancet, (1991) Vol. 337, No. 8735, pp. 234.  
 ISSN: 0140-6736 CODEN: LANCAO  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Letter  
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 022 Human Genetics  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 16 Dec 1991  
 Last Updated on STN: 16 Dec 1991  
 CONTROLLED TERM: Medical Descriptors:  
 adult  
 case report  
 \*cystic fibrosis: DI, diagnosis  
 \*cystic fibrosis: DT, drug therapy  
 \*genetic analysis  
 \*heterozygote  
 human  
 letter  
 male  
 priority journal  
 CONTROLLED TERM: Drug Descriptors:  
 \*antihistaminic agent  
 \*cholinergic receptor blocking agent  
 \*corticosteroid  
 \*tricyclic antidepressant agent

L91 ANSWER 49 OF 49 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1968:78186 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV19684900078189; BA49:78189  
 TITLE: letter asthmatic woman.  
 Original Title: Amitriptyline and sputum viscosity.  
 AUTHOR(S): BAILLIE, RITA M.  
 CORPORATE SOURCE: Monyhull Hosp., Birmingham, Engl., UK  
 SOURCE: LANCET, (1967) Vol. 2, No. 7511, pp. 369-370.  
 DOCUMENT TYPE: Article  
 FILE SEGMENT: BA  
 LANGUAGE: Unavailable  
 ENTRY DATE: Entered STN: May 2007

10/524815

Last Updated on STN: May 2007

ABSTRACT:An asthmatic woman had in-creased sputum viscosity when given 150 mg amitriptyline daily for depression. When the dosage was halved, the sputum became more fluid. A 16 year old girl with fibrocystic disease of the pancreas and associated chronic chest infection given amitriptyline, had the same results.

CONCEPT CODE: Pharmacology - Immunological processes and allergy 22018

INDEX TERMS: Major Concepts

Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms

pancreas: digestive system, endocrine system; sputum

INDEX TERMS: Diseases

chronic chest infection: disease, Infection

INDEX TERMS: Diseases

infection: infectious disease

Infection (MeSH)

INDEX TERMS: Chemicals & Biochemicals

amitriptyline

REGISTRY NUMBER: 50-48-6 (amitriptyline)

10/524815

=> file registry

FILE 'REGISTRY' ENTERED AT 11:28:47 ON 14 OCT 2009  
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DICTIONARY FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6

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<http://www.cas.org/support/stngen/stdoc/properties.html>

=> file zcaplus

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FILE COVERS 1907 - 14 Oct 2009 VOL 151 ISS 16  
FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

ZCAplus now includes complete International Patent Classification (IPC)  
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L74

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L27      5892 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  CFTR/BI
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          OR BAC OR PKT OR PAC)/RL) AND L63

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=> d ibib abs hitind hitstr L74 1-7

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L74  ANSWER 1 OF 7  ZCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:      2005:99226  ZCAPLUS  Full-text
DOCUMENT NUMBER:      142:197859
TITLE:                Preparation of dibenzo[b,f]furan-1-carboxamides,
                      9H-carbazole-4-carboxamides, and
                      dibenzo[b,d]thiophene-4-carboxamides as PDE4
                      inhibitors for the treatment of inflammatory and

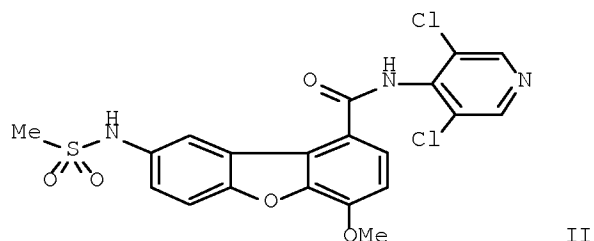
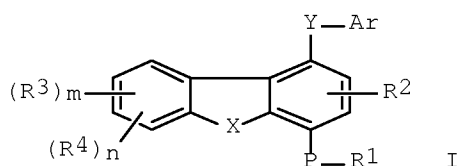
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10/524815

allergic disorders  
 INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant A.;  
 Lakdawala, Aftab D.; Karunakaran, Usha  
 PATENT ASSIGNEE(S): Glenmark Pharmaceuticals, Inc. USA, USA  
 SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of Appl.  
 No. PCT/IB04/000355.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050027129	A1	20050203	US 2004-821642	20040409 <--
US 7223789	B2	20070529		
IN 2003MU00363	A	20050304	IN 2003-MU363	20030411 <--
WO 2004089940	A1	20041021	WO 2004-IB355	20040211 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ZA 2005008240	A	20060531	ZA 2005-8240	20051012 <--
US 20070105854	A1	20070510	US 2006-536434	20060928 <--
US 7384962	B2	20080610		
US 20070105855	A1	20070510	US 2006-536448	20060928 <--
US 7393846	B2	20080701		
US 20090182143	A1	20090716	US 2008-131286	20080602 <--
PRIORITY APPLN. INFO.:				
			IN 2003-MU363	A 20030411 <--
			US 2003-519967P	P 20031113 <--
			WO 2004-IB355	A2 20040211
			US 2004-821642	A3 20040409
			US 2006-536434	A1 20060928

OTHER SOURCE(S): MARPAT 142:197859  
 GI



- AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6 (R5, R6 = H, alkyl, cycloalkyl, etc.), heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SOO-2, NRa; Y = CONR7, NR7SOO-2, SOO-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; Ra = H, alkyl, cycloalkyl, etc.; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1-carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).
- IC ICM C07D333-76  
ICS C07D209-82; C07D307-91
- INCL 549048000; 548444000; 549460000
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide  
prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic;  
**tricyclic** heterocycle prepn phosphodiesterase 4 inhibitor  
antiinflammatory antiallergic antidiabetic
- IT Inflammation  
(Crohn's disease, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease  
(Crohn's, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Eye, disease  
Inflammation  
(allergic conjunctivitis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Inflammation  
Nose, disease  
(allergic rhinitis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(allergic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis  
(atopic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease  
(cerebrovascular, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and



- inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease  
Inflammation  
(chronic bronchitis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease  
(chronic obstructive pulmonary disease, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(chronic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(dementia, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(depression, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma  
(eosinophilic, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease  
(failure, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
(inflammation, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease  
Heart, disease  
Intestine, disease  
Joint, anatomical  
Lung, disease  
Skin, disease  
(inflammatory conditions or immune disorders, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease  
(inflammatory, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus  
(insulin-resistant, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
Kidney, disease  
(nephritis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors  
Alzheimer's disease  
Anti-Alzheimer's agents  
Anti-inflammatory agents

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- Antiarthritics
- Antiasthmatics
- Antidepressants
- Antidiabetic agents
- Antirheumatic agents
- Cardiovascular agents
- Drug delivery systems
- Human
- Immunomodulators
- Nervous system agents
  - (preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT **Tricyclic** compounds
  - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
  - (preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
- Gout
- Osteoarthritis
  - (rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
  - Spinal column, disease
    - (spondylitis, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
- Amnesia
- Asthma
- Central nervous system, disease
  - Cystic fibrosis**
- Immune disease
- Inflammation
- Multiple sclerosis
- Psoriasis
- Respiratory distress syndrome
- Rheumatoid arthritis
- Shock (circulatory collapse)
- Urticaria
  - (treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
  - Intestine, disease
    - (ulcerative colitis, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease
  - Inflammation
    - (uveitis; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
- 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

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N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
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778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
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778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
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N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
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778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-  
oxoethylamino)dibenzo[b,d]furan-1-carboxamide  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN  
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4  
inhibitors for treatment of immune and inflammatory disorders and  
insulin resistant diabetes)

IT 778576-35-5P 778576-36-6P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
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778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-  
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salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[[ (fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
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[[ (isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
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[[ (diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
[(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (N-  
methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide

hydrochloride 778576-56-0P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P  
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, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-59-3P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-60-6P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-61-7P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-63-9P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778576-64-0P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-65-1P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-67-3P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-68-4P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-71-9P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-73-1P,  
N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P,  
N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P,  
N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-83-3P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-84-4P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-85-5P,  
N-(Pyridin-3-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P  
778576-88-8P 778576-89-9P,  
N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-91-3P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (2-hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-93-5P,  
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,  
N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-carboxamide 778576-95-7P,  
N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[[ (methylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-96-8P,  
N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[[ (ethylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-97-9P,  
N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-carbazole-4-carboxamide 778576-98-0P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-99-1P 778577-06-3P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt 778577-07-4P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778581-69-4P  
RL: FAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(PDE4 inhibitor; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT 2973-58-2P, 2-Bromoiso vanillin 19688-46-1P,  
 3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P,  
 3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P,  
 2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P,  
 4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P,  
 4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P,  
 4-Cyclopentyloxy-3-hydroxybenzaldehyde 685873-89-6P,  
 2-Bromo-4-cyclopentyloxy-3-hydroxybenzaldehyde 685873-90-9P,  
 2-Bromo-4-cyclopentyloxy-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P,  
 4-Cyclopentyloxy-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P,  
 4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P,  
 4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P,  
 4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid  
 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P,  
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-  
 carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-  
 8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-  
 carboxamide 778576-29-7P, Methyl  
 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl  
 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl  
 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P,  
 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-  
 carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-  
 carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-  
 carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-  
 nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P,  
 N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-  
 carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P  
 778577-04-1P 778577-05-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(intermediate; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT 9036-21-9, Phosphodiesterase type 4  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 836627-26-0P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
 THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9,

4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7,  
 N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9,  
 Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9,  
 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5,  
 2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl  
 isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isovanillin  
 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8,  
 Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8,  
 Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride  
 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6,  
 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7,  
 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl  
 3-amino-4-methoxybenzoate 778576-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tricyclic heterocycles as PDE4 inhibitors for  
 treatment of immune and inflammatory disorders and insulin resistant  
 diabetes)

IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-  
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-  
 ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-  
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide

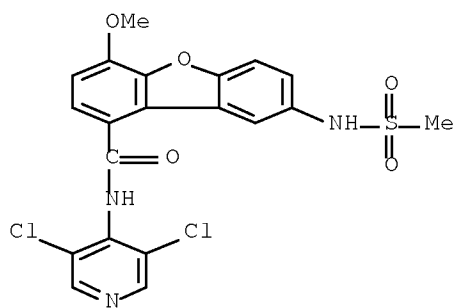
RL: PAC (Pharmacological activity); RCT (Reactant); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4  
 inhibitors for treatment of immune and inflammatory disorders and  
 insulin resistant diabetes)

RN 778576-34-4 ZCAPLUS

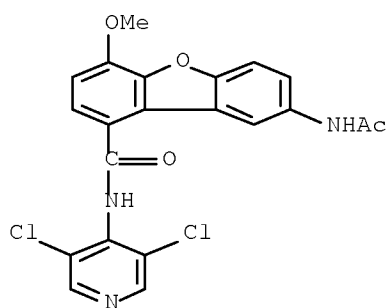
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-  
 [(methylsulfonyl)amino]- (CA INDEX NAME)

10/524815



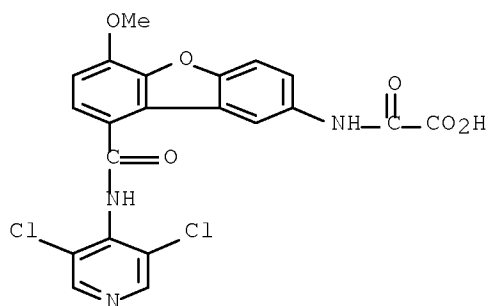
RN 778576-37-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-41-3 ZCAPLUS

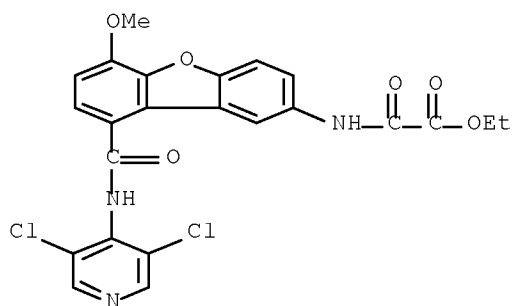
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)



RN 778576-42-4 ZCAPLUS

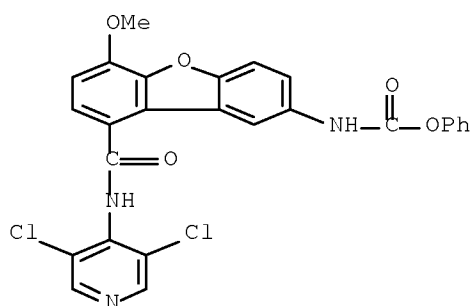
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)

10/524815



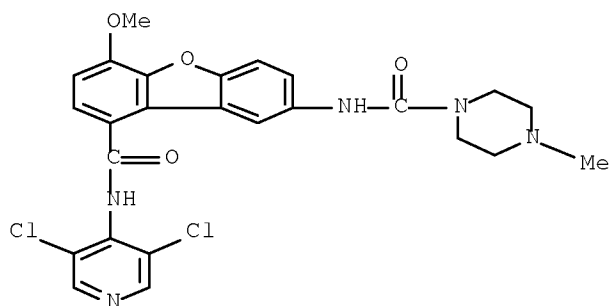
RN 778576-49-1 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, phenyl ester (9CI) (CA INDEX NAME)



RN 778576-54-8 ZCAPLUS

CN 1-Piperazinecarboxamide, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl- (CA INDEX NAME)

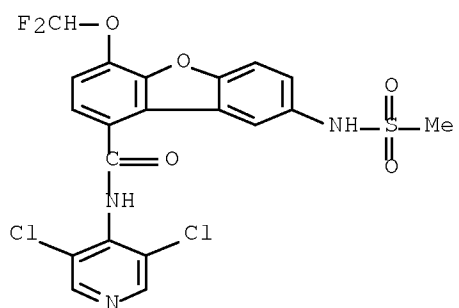


RN 778576-62-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]- (CA INDEX NAME)

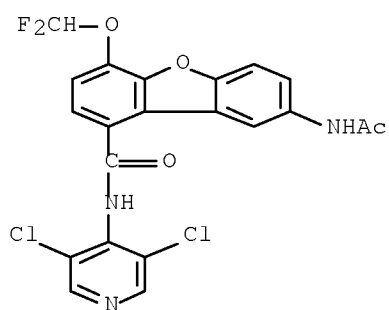


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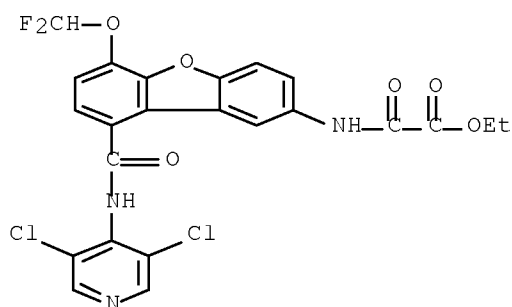
RN 778576-66-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-69-5 ZCAPLUS

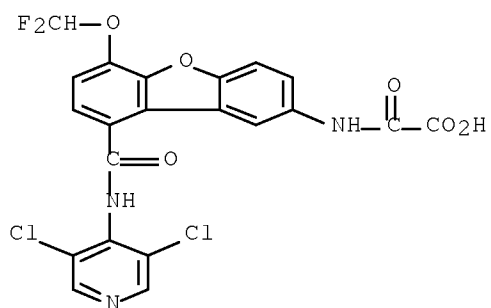
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)



RN 778576-70-8 ZCAPLUS

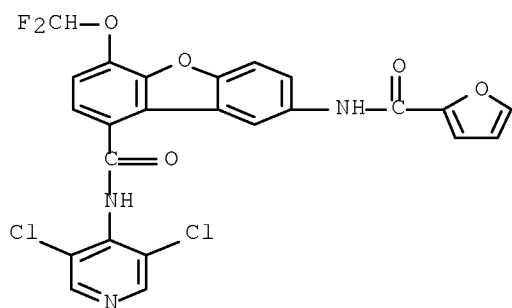
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)

10/524815



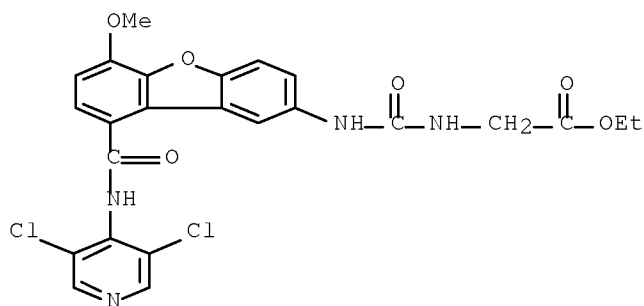
RN 778576-72-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]- (CA INDEX NAME)



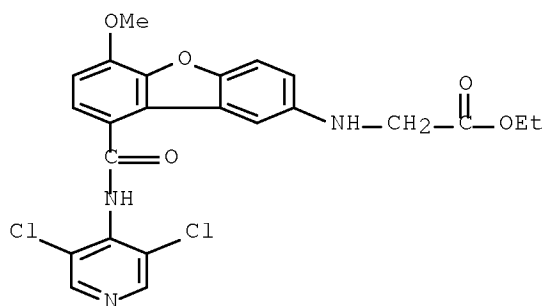
RN 778576-90-2 ZCAPLUS

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]-, ethyl ester (CA INDEX NAME)



RN 778576-92-4 ZCAPLUS

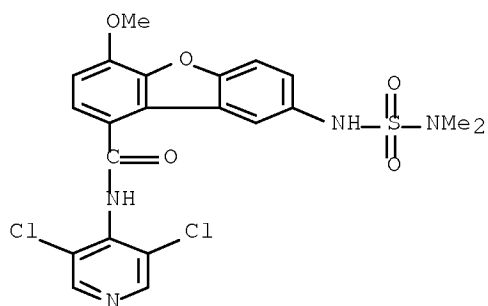
CN Glycine, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, ethyl ester (CA INDEX NAME)



IT 778576-35-5P 778576-36-6P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (3-  
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-  
 butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium  
 salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-48-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (N-  
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 hydrochloride 778576-56-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (4-hydroxypiperidin-1-  
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (morpholin-4-  
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-60-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-61-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-

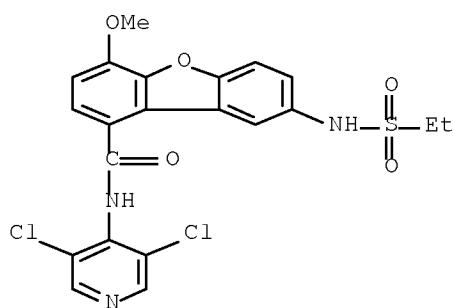
[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-65-1P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium  
 salt 778576-73-1P, N-Phenyl-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P,  
 N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-80-0P, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
 carboxamide 778576-83-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P  
 778576-88-8P 778576-89-9P,  
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-  
 hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-  
 2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-  
 carboxamide 778576-95-7P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-  
 9H-carbazole-4-carboxamide 778576-96-8P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-  
 9H-carbazole-4-carboxamide 778576-97-9P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-  
 carbazole-4-carboxamide 778576-98-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt  
 778576-99-1P 778577-06-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide sodium salt  
 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778581-69-4P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
 THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4  
 inhibitors for treatment of immune and inflammatory disorders and  
 insulin resistant diabetes)  
 RN 778576-35-5 ZCAPLUS  
 CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-  
 [[(dimethylamino)sulfonyl]amino]-4-methoxy- (CA INDEX NAME)

10/524815



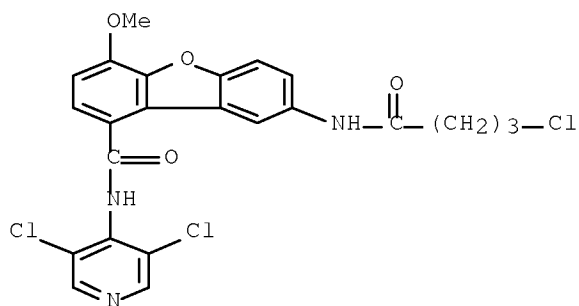
RN 778576-36-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(ethylsulfonyl)amino]-4-methoxy- (CA INDEX NAME)



RN 778576-38-8 ZCAPLUS

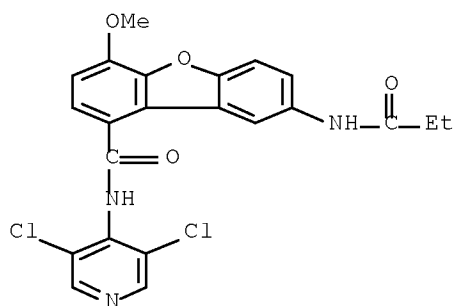
CN 1-Dibenzofurancarboxamide, 8-[(4-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-39-9 ZCAPLUS

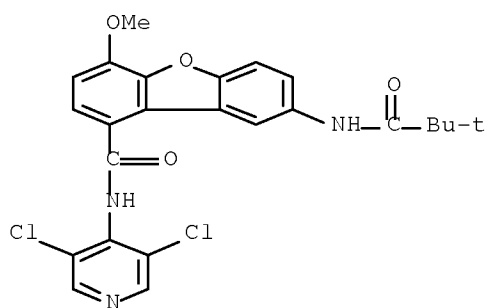
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[(1-oxopropyl)amino]- (CA INDEX NAME)

10/524815



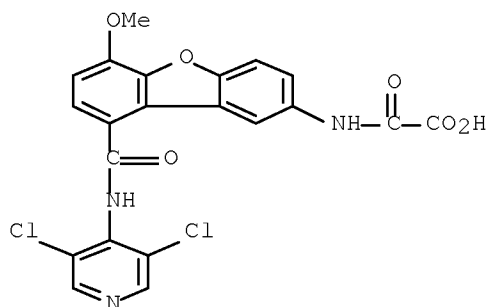
RN 778576-40-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2,2-dimethyl-1-oxopropyl)amino]-4-methoxy- (CA INDEX NAME)



RN 778576-43-5 ZCAPLUS

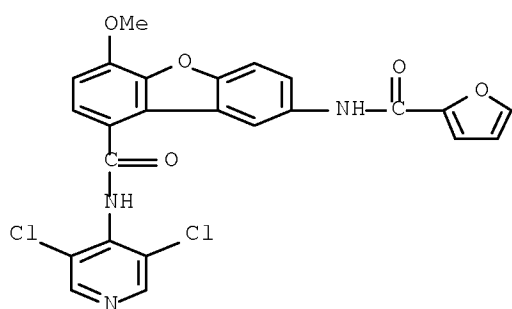
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:1) (CA INDEX NAME)



RN 778576-44-6 ZCAPLUS

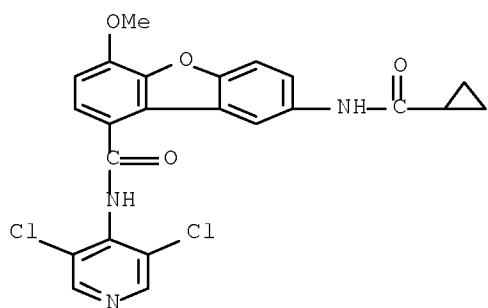
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2-furanylcarbonyl)amino]-4-methoxy- (CA INDEX NAME)

10/524815



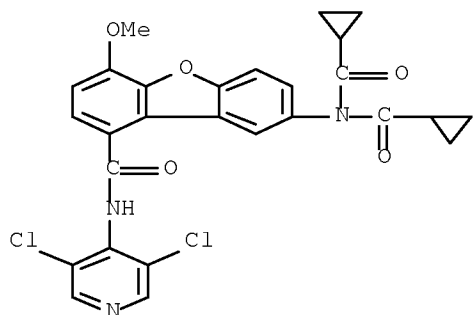
RN 778576-45-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-46-8 ZCAPLUS

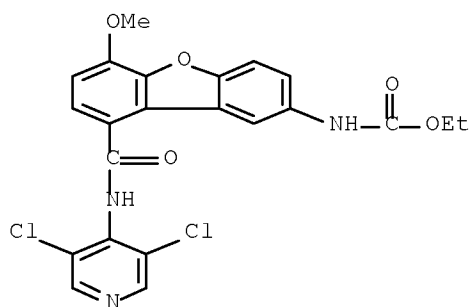
CN 1-Dibenzofurancarboxamide, 8-bis[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-47-9 ZCAPLUS

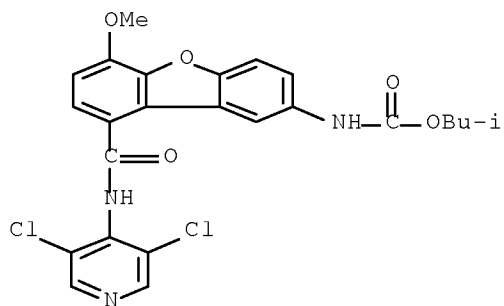
CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, ethyl ester (9CI) (CA INDEX NAME)

10/524815



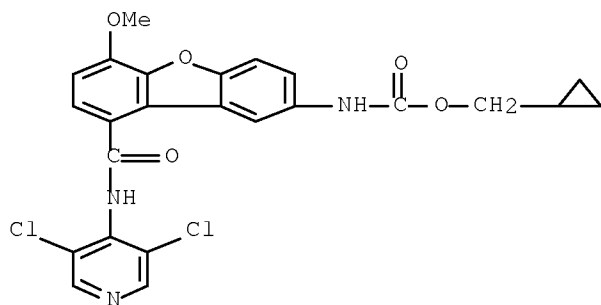
RN 778576-48-0 ZCAPLUS

CN Carbamic acid, [9-[[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



RN 778576-50-4 ZCAPLUS

CN Carbamic acid, [9-[[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, cyclopropylmethyl ester (9CI) (CA INDEX NAME)

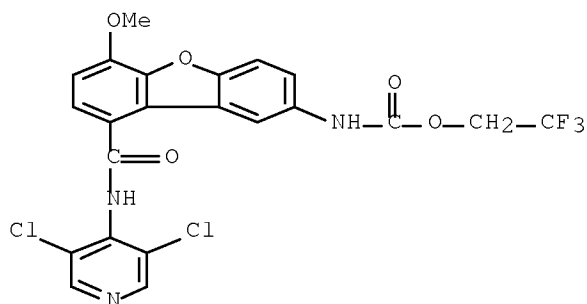


RN 778576-51-5 ZCAPLUS

CN Carbamic acid, [9-[[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2,2,2-trifluoroethyl ester (9CI) (CA INDEX NAME)

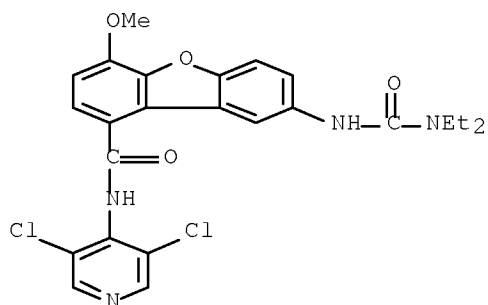


10/524815



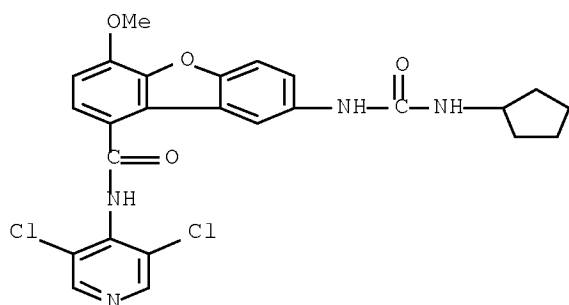
RN 778576-52-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[[(diethylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-53-7 ZCAPLUS

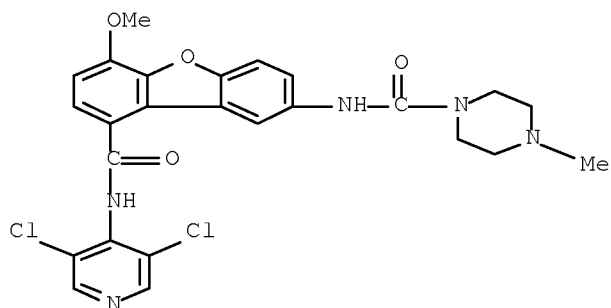
CN 1-Dibenzofurancarboxamide, 8-[[[(cyclopentylamino)carbonyl]amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-55-9 ZCAPLUS

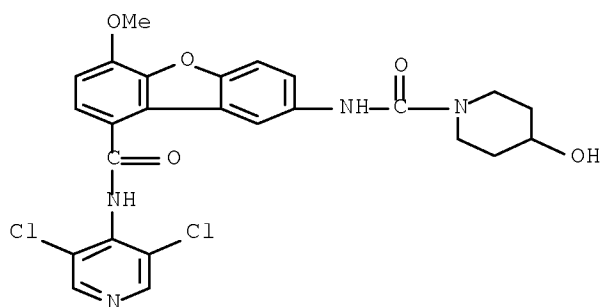
CN 1-Piperazinecarboxamide, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl-, hydrochloride (1:1) (CA INDEX NAME)

10/524815



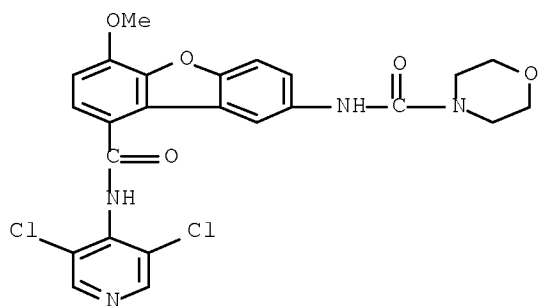
RN 778576-56-0 ZCAPLUS

CN 1-Piperidinecarboxamide, N-[9-[[[3,5-dichloro-4-pyridinyl]amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-hydroxy- (CA INDEX NAME)



RN 778576-57-1 ZCAPLUS

CN 4-Morpholinecarboxamide, N-[9-[[[3,5-dichloro-4-pyridinyl]amino]carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)

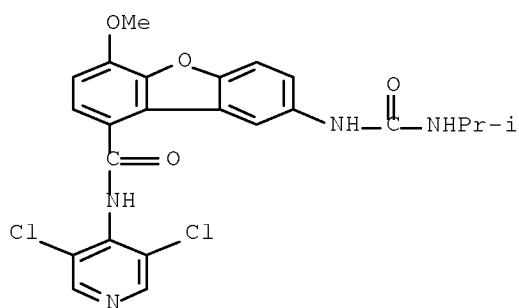


RN 778576-58-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[[[1-(4-morpholinyl)carbonyl]amino]carbonyl]- (CA INDEX NAME)

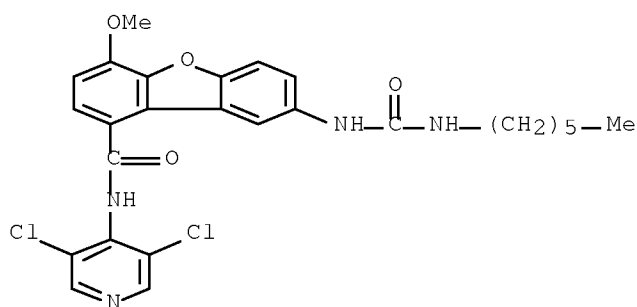
10/524815

methylethyl)amino]carbonyl]amino]- (CA INDEX NAME)



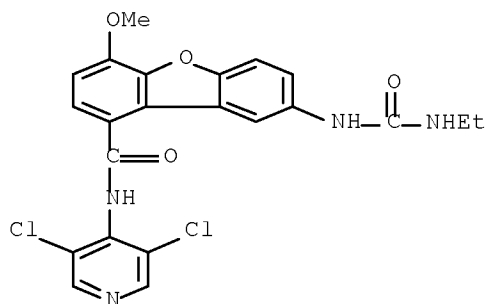
RN 778576-59-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[ (hexylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-60-6 ZCAPLUS

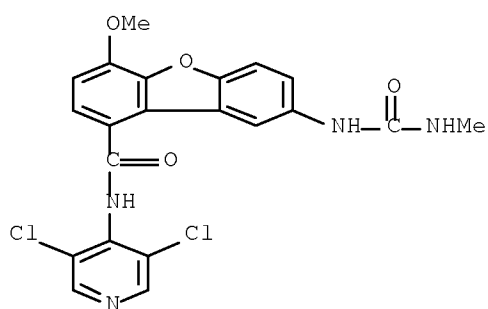
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[ (ethylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-61-7 ZCAPLUS

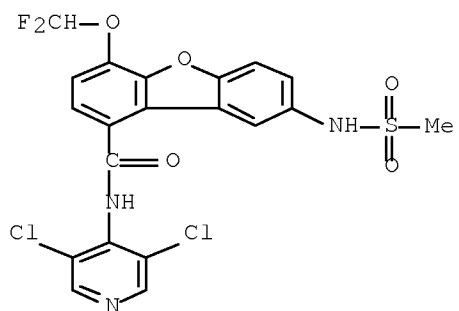
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[[ (methylamino)carbonyl]amino]- (CA INDEX NAME)

10/524815



RN 778576-63-9 ZCAPLUS

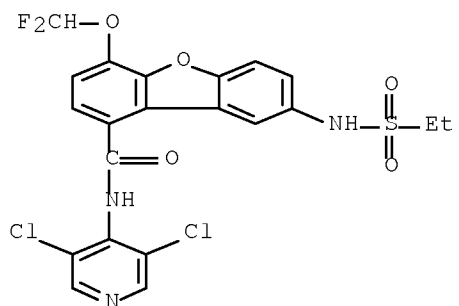
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:1) (CA INDEX NAME)



● Na

RN 778576-64-0 ZCAPLUS

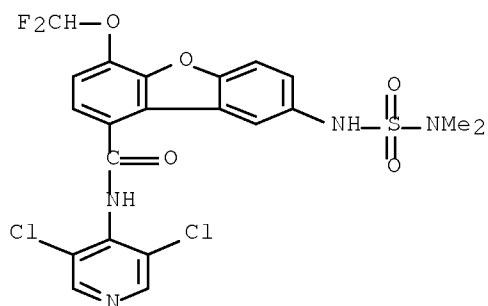
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(ethylsulfonyl)amino]- (CA INDEX NAME)



10/524815

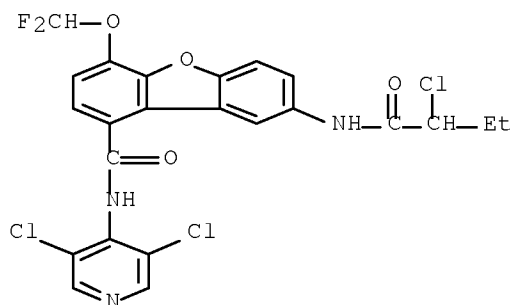
RN 778576-65-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[[ (dimethylamino)sulfonyl]amino]- (CA INDEX NAME)



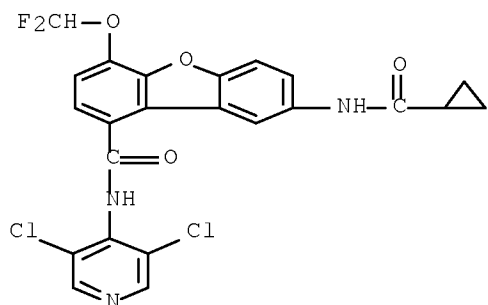
RN 778576-67-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(2-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-68-4 ZCAPLUS

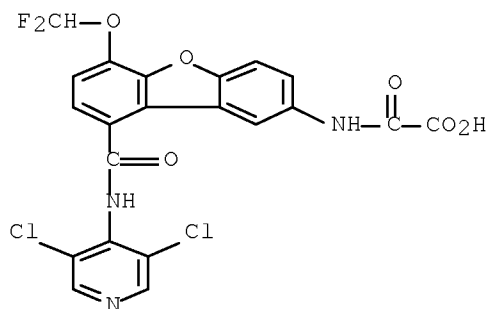
CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-71-9 ZCAPLUS

10/524815

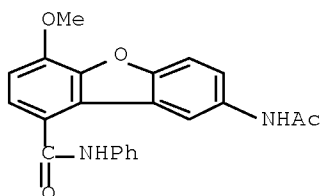
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:2) (CA INDEX NAME)



●2 Na

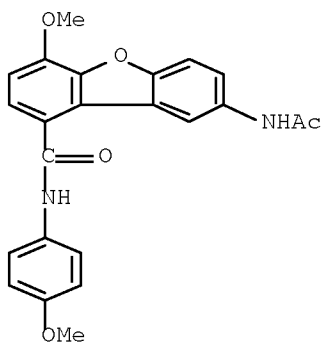
RN 778576-73-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-phenyl- (CA INDEX NAME)



RN 778576-77-5 ZCAPLUS

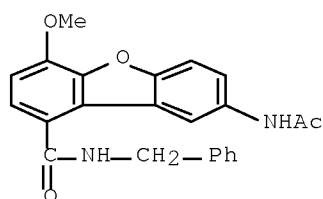
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



10/524815

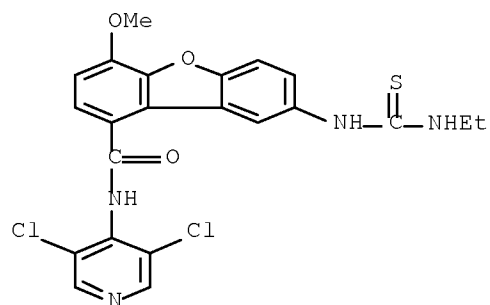
RN 778576-80-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(phenylmethyl)-  
(CA INDEX NAME)



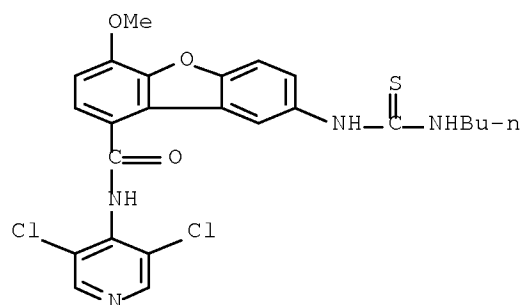
RN 778576-83-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-  
[[ (ethylamino)thioxomethyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-84-4 ZCAPLUS

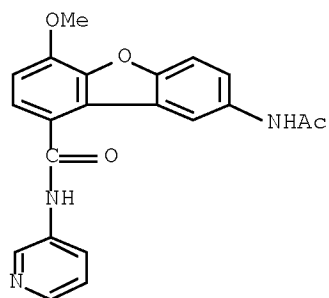
CN 1-Dibenzofurancarboxamide, 8-[[ (butylamino)thioxomethyl]amino]-N-(3,5-  
dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-85-5 ZCAPLUS

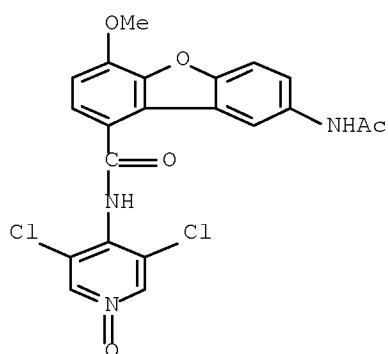
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-3-pyridinyl- (CA  
INDEX NAME)

10/524815



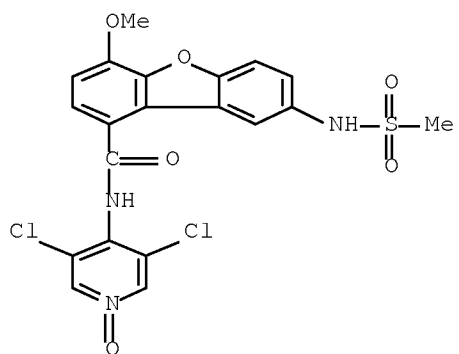
RN 778576-87-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-88-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-8-[(methylsulfonyl)amino]- (CA INDEX NAME)

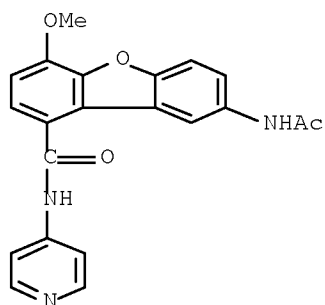


RN 778576-89-9 ZCAPLUS



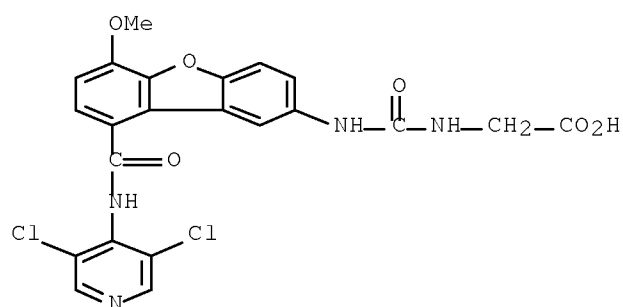
10/524815

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



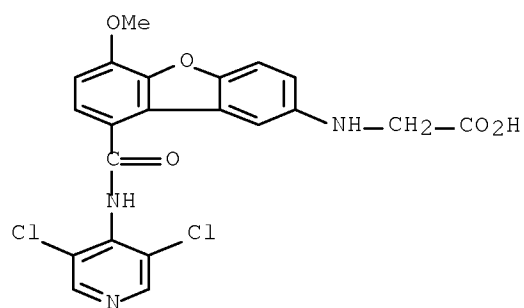
RN 778576-91-3 ZCAPLUS

CN Glycine, N-[[[9-[[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]- (CA INDEX NAME)



RN 778576-93-5 ZCAPLUS

CN Glycine, N-[9-[[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)

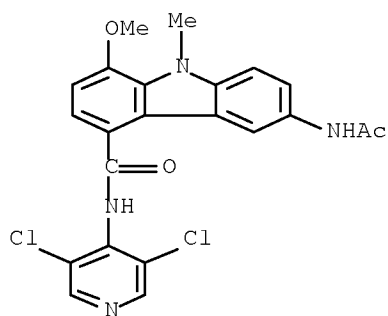


RN 778576-94-6 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-1-

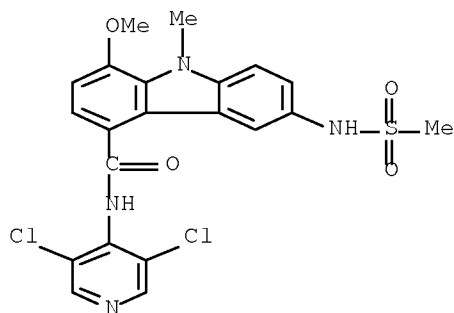
10/524815

methoxy-9-methyl- (CA INDEX NAME)



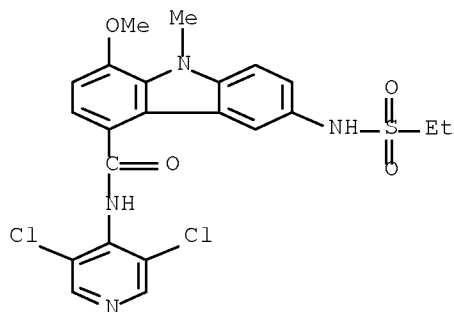
RN 778576-95-7 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl-6-[(methanesulfonyl)amino]- (CA INDEX NAME)



RN 778576-96-8 ZCAPLUS

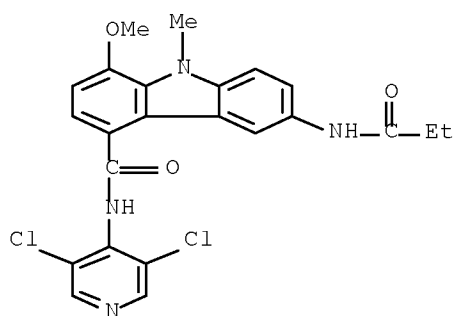
CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl-6-[(ethanesulfonyl)amino]- (CA INDEX NAME)



RN 778576-97-9 ZCAPLUS

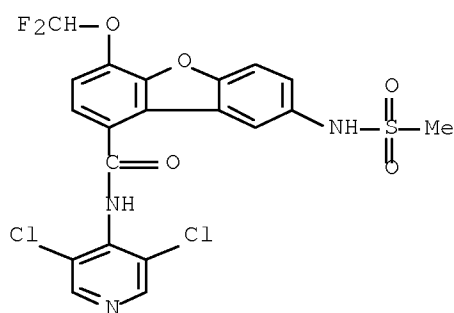
CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl-6-[(1-oxopropyl)amino]- (CA INDEX NAME)

10/524815



RN 778576-98-0 ZCAPLUS

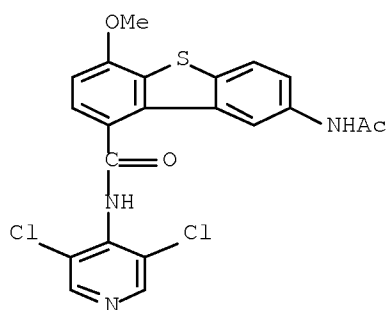
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:2) (CA INDEX NAME)



●2 Na

RN 778576-99-1 ZCAPLUS

CN 1-Dibenzothienecarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy-, sodium salt (1:2) (CA INDEX NAME)

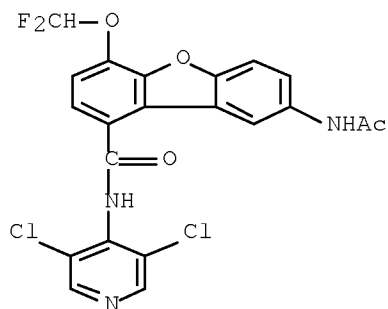


●2 Na

10/524815

RN 778577-06-3 ZCAPLUS

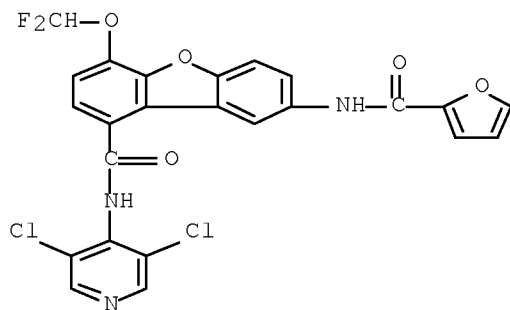
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-, sodium salt (1:1) (CA INDEX NAME)



● Na

RN 778577-07-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]-, sodium salt (1:1) (CA INDEX NAME)

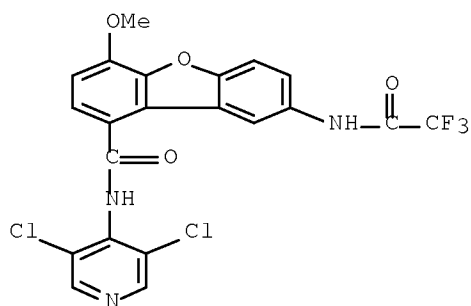


● Na

RN 778581-69-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[(2,2,2-trifluoroacetyl)amino]- (CA INDEX NAME)

10/524815

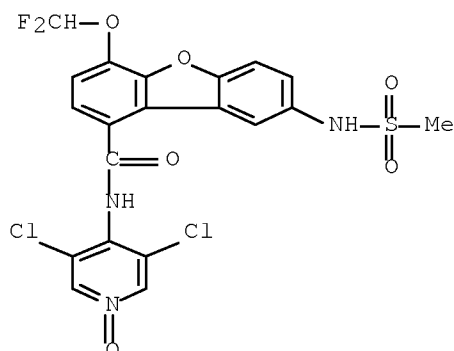


IT 836627-26-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(preparation of tricyclic heterocycles as PDE4 inhibitors for  
treatment of immune and inflammatory disorders and insulin resistant  
diabetes)

RN 836627-26-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-  
(difluoromethoxy)-8-[(methylsulfonyl)amino]- (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 2 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:1127375 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:74464

TITLE: Preparation of tricyclic compounds useful for the  
treatment of inflammatory and allergic disorders

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram;  
Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

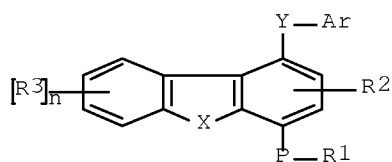
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

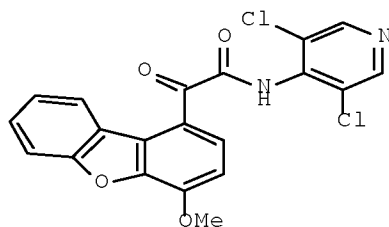
10/524815

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111044	A1	20041223	WO 2004-IB1643	20040616 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00631	A	20050211	IN 2003-MU631	20030617 <--
PRIORITY APPLN. INFO.:			IN 2003-MU631	A 20030617 <--
OTHER SOURCE(S):			MARPAT 142:74464	
GI				



I



II

AB The title compds. I [R1-R3 = H, alkyl, cycloalkyl, aryl, etc.; n = 0-4; X = O, S(O)m, NRA (wherein m = 0-2; Ra = H, alkyl, cycloalkyl, etc.); P = O, S; Ar = (un)substituted aryl, arylalkyl, heterocyclyl, heteroaryl; Y = C(A)C(B)NR4 (wherein A, B = O, S, NRA; R4 = H, alkyl, OH, aryl, etc.)] which are novel phosphodiesterase type 4 (PDE4) inhibitors useful for the treatment of inflammatory and allergic disorders, were prepared Thus, reacting 2-(4-methoxydibenzo[b,f]furan-1-yl)-2-oxoacetic acid (preparation given) with 4-amino-3,5-dichloropyridine afforded II which showed IC50 of 184 nM against PDE4.

IC ICM C07D405-12  
ICS A61K031-343

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1

ST tricyclic compd prepn phosphodiesterase 4 PDE4 inhibitor  
antiinflammatory; dibenzofuranyloxoacetamide prepn phosphodiesterase 4  
PDE4 inhibitor antiinflammatory allergy asthma

IT Allergy  
Alzheimer's disease  
Amnesia  
Asthma  
Central nervous system, disease  
Cystic fibrosis

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Eczema  
Gout  
Immune disease  
Inflammation  
Multiple sclerosis  
Osteoarthritis  
Psoriasis  
Rheumatoid arthritis  
Shock (circulatory collapse)  
Urticaria

(treating; preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors

for

the treatment of inflammatory and allergic disorders)

IT 815586-07-3P 815586-08-4P 815586-09-5P  
815586-10-8P 815586-11-9P 815586-12-0P  
815586-13-1P 815586-14-2P 815586-15-3P  
815586-16-4P 815586-17-5P 815586-18-6P  
815586-19-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors for the  
treatment of inflammatory and allergic disorders)

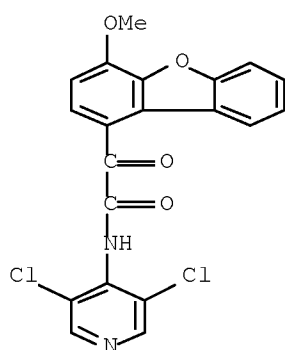
IT 815586-07-3P 815586-08-4P 815586-09-5P  
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815586-16-4P 815586-17-5P 815586-18-6P  
815586-19-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors for the  
treatment of inflammatory and allergic disorders)

RN 815586-07-3 ZCAPLUS

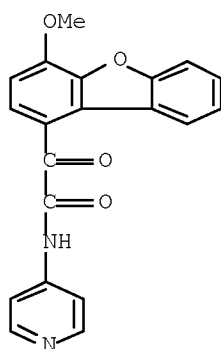
CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- $\alpha$ -  
oxo- (CA INDEX NAME)



RN 815586-08-4 ZCAPLUS

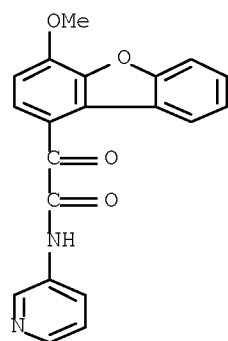
CN 1-Dibenzofuranacetamide, 4-methoxy- $\alpha$ -oxo-N-4-pyridinyl- (CA INDEX  
NAME)

10/524815



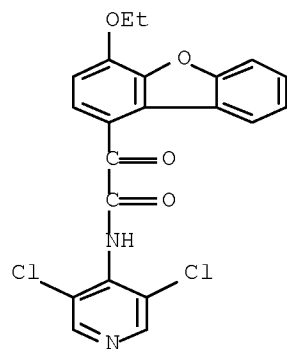
RN 815586-09-5 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-methoxy- $\alpha$ -oxo-N-3-pyridinyl- (CA INDEX NAME)



RN 815586-10-8 ZCAPLUS

CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-ethoxy- $\alpha$ -oxo- (CA INDEX NAME)



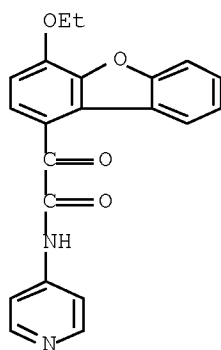
RN 815586-11-9 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-ethoxy- $\alpha$ -oxo-N-4-pyridinyl- (CA INDEX NAME)



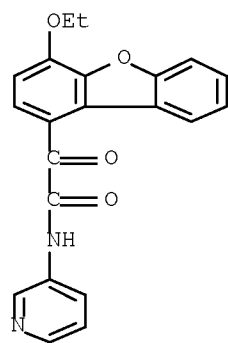
10/524815

NAME)



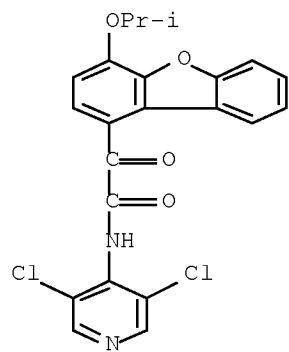
RN 815586-12-0 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-ethoxy- $\alpha$ -oxo-N-3-pyridinyl- (CA INDEX NAME)



RN 815586-13-1 ZCAPLUS

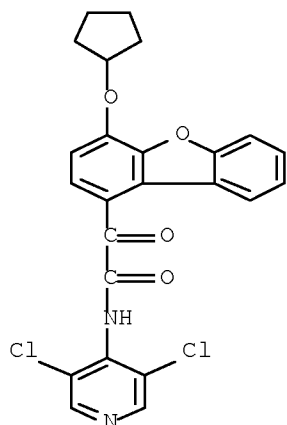
CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-(1-methylethoxy)- $\alpha$ -oxo- (CA INDEX NAME)



10/524815

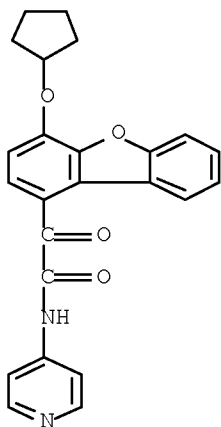
RN 815586-14-2 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-(cyclopentyloxy)-N-(3,5-dichloro-4-pyridinyl)- $\alpha$ -oxo- (CA INDEX NAME)



RN 815586-15-3 ZCAPLUS

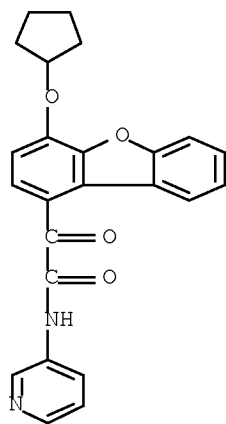
CN 1-Dibenzofuranacetamide, 4-(cyclopentyloxy)- $\alpha$ -oxo-N-4-pyridinyl- (CA INDEX NAME)



RN 815586-16-4 ZCAPLUS

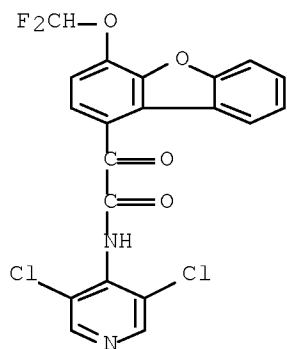
CN 1-Dibenzofuranacetamide, 4-(cyclopentyloxy)- $\alpha$ -oxo-N-3-pyridinyl- (CA INDEX NAME)

10/524815



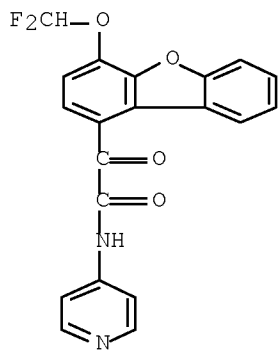
RN 815586-17-5 ZCAPLUS

CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-  
 $\alpha$ -oxo- (CA INDEX NAME)



RN 815586-18-6 ZCAPLUS

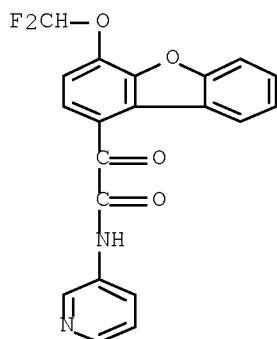
CN 1-Dibenzofuranacetamide, 4-(difluoromethoxy)- $\alpha$ -oxo-N-4-pyridinyl-  
(CA INDEX NAME)



10/524815

RN 815586-19-7 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-(difluoromethoxy)- $\alpha$ -oxo-N-3-pyridinyl-  
(CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)  
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 3 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:878393 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:366121

TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides,  
9H-carbazole-4-carboxamides, and  
dibenzo[b,d]thiophene-4-carboxamides as PDE4  
inhibitors for the treatment of inflammatory and  
allergic disorders

INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant Atmaram;  
Lakdawala, Aftab Dawoodbhai; Karaunakaran, Usha

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004089940	A1	20041021	WO 2004-IB355	20040211 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
IN 2003MU00363	A	20050304	IN 2003-MU363	20030411 <--
AU 2004228453	A1	20041021	AU 2004-228453	20040211 <--

10/524815

CA 2522023	A1	20041021	CA 2004-2522023	20040211 <--
EP 1620429	A1	20060201	EP 2004-710093	20040211 <--
EP 1620429	B1	20090401		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

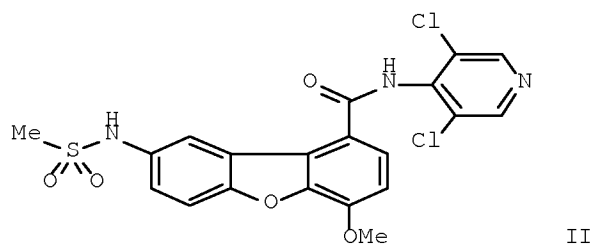
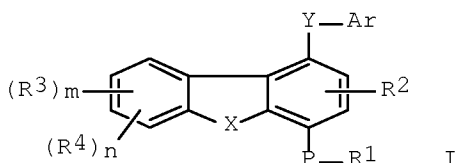
BR 2004009747	A	20060509	BR 2004-9747	20040211 <--
CN 1829711	A	20060906	CN 2004-80016048	20040211 <--
JP 2006522789	T	20061005	JP 2006-506259	20040211 <--
NZ 542882	A	20071026	NZ 2004-542882	20040211 <--
AT 427308	T	20090415	AT 2004-710093	20040211 <--
ES 2320888	T3	20090529	ES 2004-710093	20040211 <--
AP 2008	A	20090630	AP 2005-3424	20040211 <--
US 20050027129	A1	20050203	US 2004-821642	20040409 <--
US 7223789	B2	20070529		
MX 2005010948	A	20060531	MX 2005-10948	20051011 <--
ZA 2005008240	A	20060531	ZA 2005-8240	20051012 <--
NO 2005005316	A	20060111	NO 2005-5316	20051110 <--
US 20070105854	A1	20070510	US 2006-536434	20060928 <--
US 7384962	B2	20080610		
US 20070105855	A1	20070510	US 2006-536448	20060928 <--
US 7393846	B2	20080701		
US 20090182143	A1	20090716	US 2008-131286	20080602 <--

PRIORITY APPLN. INFO.:

IN 2003-MU363	A	20030411 <--
US 2003-519967P	P	20031113 <--
WO 2004-IB355	W	20040211
US 2004-821642	A3	20040409
US 2006-536434	A1	20060928

OTHER SOURCE(S): CASREACT 141:366121; MARPAT 141:366121

GI



AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6, heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SO0-2, NRA; Y = CONR7, NR7SO0-2, SO0-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable

salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1-carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC<sub>50</sub> of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).

- IC ICM C07D405-12
- ICS C07D405-14; C07D307-91; C07D401-12; C07D409-12; A61K031-4427; A61P029-00
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide  
prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic;  
~~tricyclic~~ heterocycle prepn phosphodiesterase 4 inhibitor  
antiinflammatory antiallergic antidiabetic
- IT Inflammation  
(Crohn's disease, treatment of; preparation of ~~tricyclic~~  
heterocycles as PDE4 inhibitors for treatment of immune and  
inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease  
(Crohn's, treatment of; preparation of ~~tricyclic~~ heterocycles as  
PDE4 inhibitors for treatment of immune and inflammatory disorders and  
insulin resistant diabetes)
- IT Allergy  
Eye, disease  
Inflammation  
(allergic conjunctivitis, rheumatoid, treatment of; preparation of  
~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of  
immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Eye, disease  
Inflammation  
(allergic conjunctivitis, treatment of; preparation of ~~tricyclic~~  
heterocycles as PDE4 inhibitors for treatment of immune and  
inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
Inflammation  
Nose, disease  
(allergic rhinitis, treatment of; preparation of ~~tricyclic~~  
heterocycles as PDE4 inhibitors for treatment of immune and  
inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(allergic, rheumatoid, treatment of; preparation of ~~tricyclic~~  
heterocycles as PDE4 inhibitors for treatment of immune and  
inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis  
(atopic, rheumatoid, treatment of; preparation of ~~tricyclic~~  
heterocycles as PDE4 inhibitors for treatment of immune and  
inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease  
(cerebrovascular, treatment of; preparation of ~~tricyclic~~  
heterocycles as PDE4 inhibitors for treatment of immune and  
inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease  
Inflammation  
(chronic bronchitis, treatment of; preparation of ~~tricyclic~~  
heterocycles as PDE4 inhibitors for treatment of immune and

- inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease  
(chronic obstructive pulmonary disease, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
(chronic, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Anti-inflammatory agents  
(chronic; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(dementia, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders  
(depression, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma  
(eosinophilic, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease  
(failure, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy  
(inflammation, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease  
Heart, disease  
Intestine, disease  
Joint, anatomical  
Lung, disease  
Skin, disease  
(inflammatory conditions or immune disorders, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease  
(inflammatory, rheumatoid, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus  
(insulin-resistant, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation  
Kidney, disease  
(nephritis, treatment of; preparation of **tricyclic** heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors  
Anti-Alzheimer's agents  
Anti-inflammatory agents  
Antiarthritics  
Antiasthmatics

- Antidepressants
- Antidiabetic agents
- Antirheumatic agents
- Cardiovascular agents
- Drug delivery systems
- Human
- Immunomodulators
- Nervous system agents
- Polymorphism (crystal)
  - (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tumor necrosis factors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT ~~Tricyclic~~ compounds
  - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
- Gout
- Osteoarthritis
  - (rheumatoid, treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
  - Spinal column, disease (spondylitis, rheumatoid, treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
- Amnesia
- Asthma
- Central nervous system, disease
- ~~Cystic fibrosis~~
- Immune disease
- Inflammation
- Multiple sclerosis
- Psoriasis
- Respiratory distress syndrome
- Rheumatoid arthritis
- Shock (circulatory collapse)
- Urticaria
  - (treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
  - Intestine, disease (ulcerative colitis, rheumatoid, treatment of; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide    778576-41-3P,



N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-  
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-  
 ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-  
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN  
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4  
 inhibitors for treatment of immune and inflammatory disorders and  
 insulin resistant diabetes)

IT 778576-35-5P 778576-36-6P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[3-  
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-  
 butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium  
 salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-48-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-  
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 hydrochloride 778576-56-0P,

N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (morpholin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-59-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-60-6P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-61-7P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-63-9P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778576-64-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-65-1P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-67-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-68-4P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-71-9P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-73-1P,  
 N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P,  
 N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P,  
 N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-83-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-84-4P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-85-5P,  
 N-(Pyridin-3-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P  
 778576-88-8P 778576-89-9P,  
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-91-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (2-hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-93-5P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-carboxamide 778576-95-7P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-96-8P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-97-9P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-carbazole-4-carboxamide 778576-98-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-99-1P 778577-06-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt 778577-07-4P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[ (fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778581-69-4P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT 2973-58-2P, 2-Bromoiso vanillin 19688-46-1P,  
 3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P,  
 3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P,  
 2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P,  
 4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P,  
 4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P,  
 4-Cyclopentyloxy-3-hydroxybenzaldehyde 685873-89-6P,  
 2-Bromo-4-cyclopentyloxy-3-hydroxybenzaldehyde 685873-90-9P,  
 2-Bromo-4-cyclopentyloxy-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P,  
 4-Cyclopentyloxy-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P,  
 4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P,  
 4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P,  
 4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid  
 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P,  
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-  
 carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-  
 8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-  
 carboxamide 778576-29-7P, Methyl  
 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl  
 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl  
 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P,  
 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-  
 carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-  
 carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-  
 carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-  
 nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P,  
 N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide  
 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide  
 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-  
 carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P  
 778577-04-1P 778577-05-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(intermediate; preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT 9036-21-9, Phosphodiesterase type 4 9040-59-9, Phosphodiesterase 1  
 9068-52-4, Phosphodiesterase type 5  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (preparation of ~~tricyclic~~ heterocycles as PDE4 inhibitors for  
 treatment of immune and inflammatory disorders and insulin resistant  
 diabetes)

- IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9,  
 4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7,  
 N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9,  
 Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9,  
 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5,  
 2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl  
 isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isovanillin  
 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8,

Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8,  
 Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride  
 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6,  
 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7,  
 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl  
 3-amino-4-methoxybenzoate 778576-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tricyclic heterocycles as PDE4 inhibitors for  
 treatment of immune and inflammatory disorders and insulin resistant  
 diabetes)

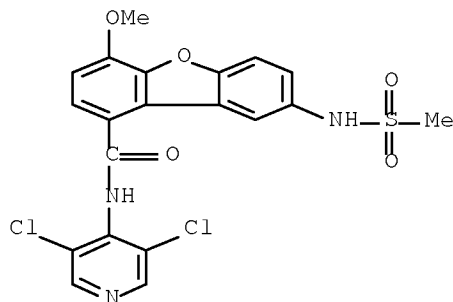
IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(phenoxyacetyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-  
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-  
 ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-  
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide

RL: PAC (Pharmacological activity); RCT (Reactant); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4  
 inhibitors for treatment of immune and inflammatory disorders and  
 insulin resistant diabetes)

RN 778576-34-4 ZCAPLUS

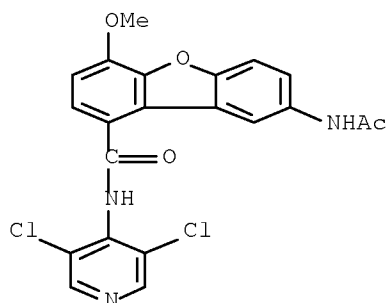
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-  
 [(methylsulfonyl)amino]- (CA INDEX NAME)



10/524815

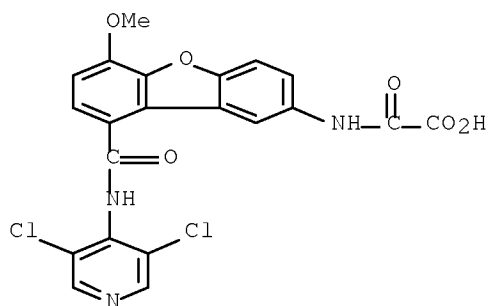
RN 778576-37-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



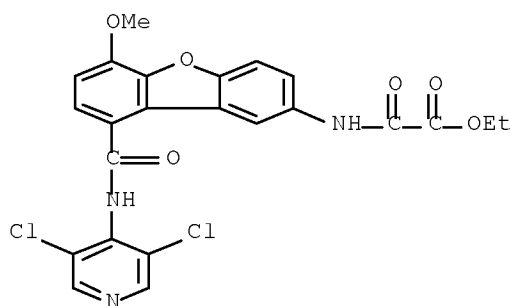
RN 778576-41-3 ZCAPLUS

CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)



RN 778576-42-4 ZCAPLUS

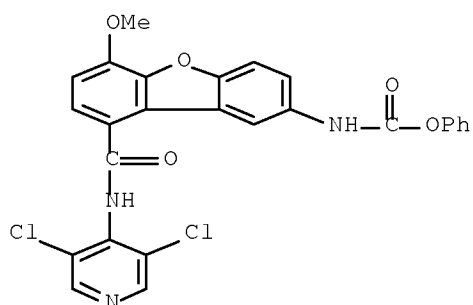
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)



10/524815

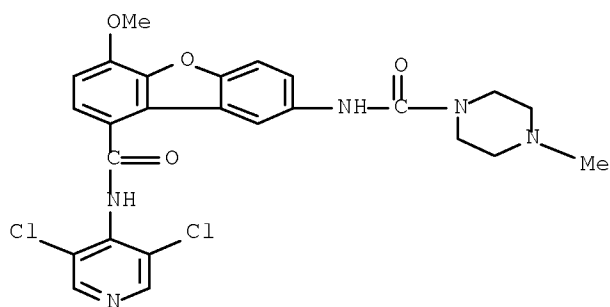
RN 778576-49-1 ZCAPLUS

CN Carbamic acid, [9-[[ (3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, phenyl ester (9CI) (CA INDEX NAME)



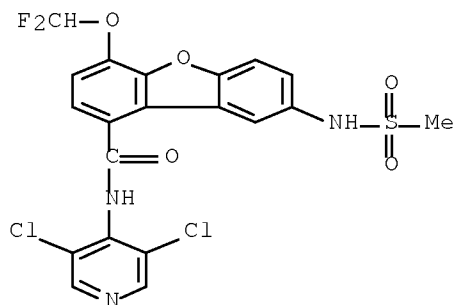
RN 778576-54-8 ZCAPLUS

CN 1-Piperazinecarboxamide, N-[9-[[ (3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl- (CA INDEX NAME)



RN 778576-62-8 ZCAPLUS

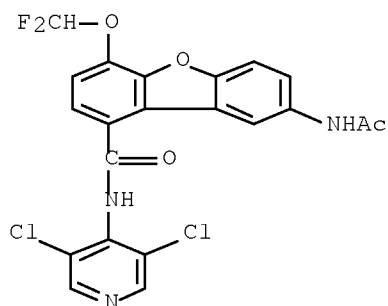
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]- (CA INDEX NAME)



10/524815

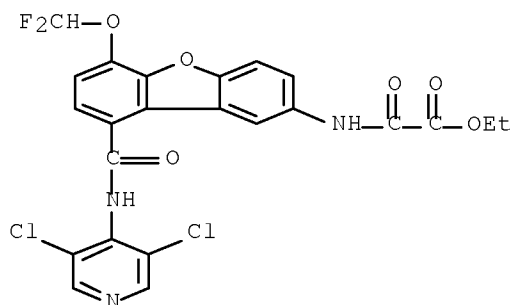
RN 778576-66-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



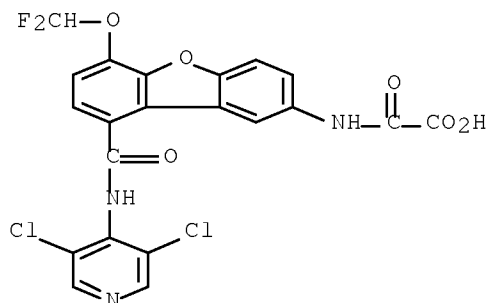
RN 778576-69-5 ZCAPLUS

CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)



RN 778576-70-8 ZCAPLUS

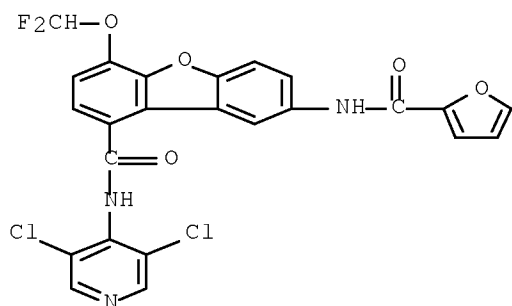
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)



10/524815

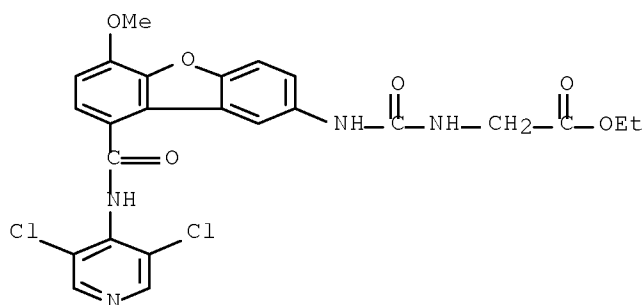
RN 778576-72-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]- (CA INDEX NAME)



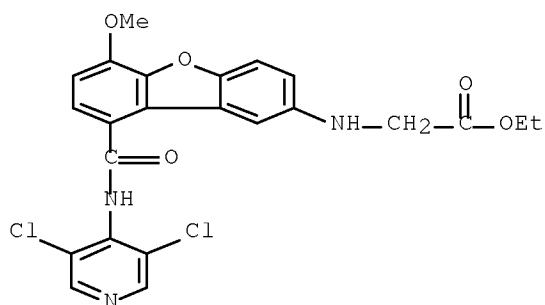
RN 778576-90-2 ZCAPLUS

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]-, ethyl ester (CA INDEX NAME)



RN 778576-92-4 ZCAPLUS

CN Glycine, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, ethyl ester (CA INDEX NAME)



IT 778576-35-5P 778576-36-6P,

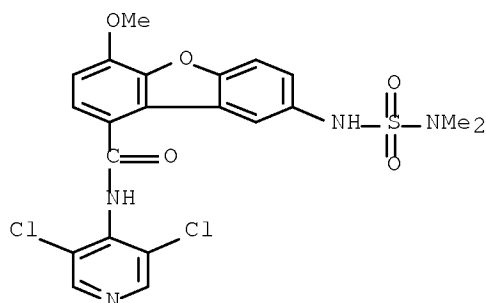


N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (3-  
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-  
 butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium  
 salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-48-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (N-  
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 hydrochloride 778576-56-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (4-hydroxypiperidin-1-  
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[ (morpholin-4-  
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P  
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-60-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-61-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-65-1P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide  
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium  
 salt 778576-73-1P, N-Phenyl-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P,  
 N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-80-0P, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-  
 carboxamide 778576-83-3P,

N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 [[(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P  
 778576-88-8P 778576-89-9P,  
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide  
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-  
 hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide  
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-  
 2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-  
 carboxamide 778576-95-7P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-  
 9H-carbazole-4-carboxamide 778576-96-8P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-  
 9H-carbazole-4-carboxamide 778576-97-9P,  
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-  
 carbazole-4-carboxamide 778576-98-0P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt  
 778576-99-1P 778577-06-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 acetamidodibenzo[b,d]furan-1-carboxamide sodium salt  
 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-  
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt  
 778581-69-4P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
 THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4  
 inhibitors for treatment of immune and inflammatory disorders and  
 insulin resistant diabetes)

RN 778576-35-5 ZCAPLUS

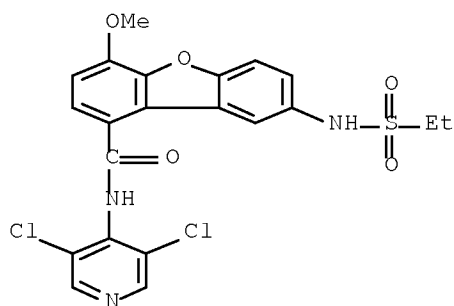
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-  
 [[(dimethylamino)sulfonyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-36-6 ZCAPLUS

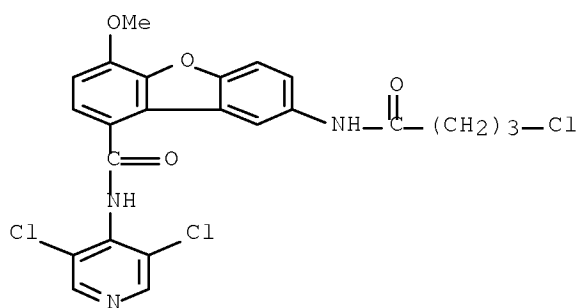
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-  
 [(ethylsulfonyl)amino]-4-methoxy- (CA INDEX NAME)

10/524815



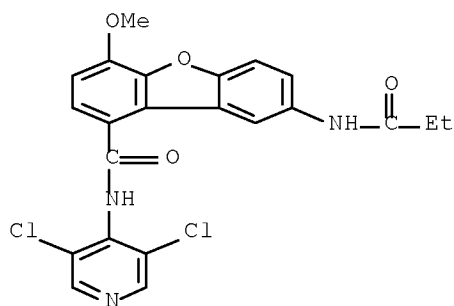
RN 778576-38-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(4-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-39-9 ZCAPLUS

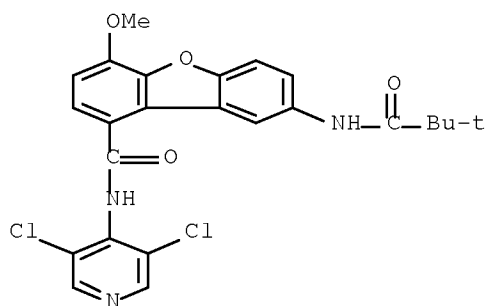
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[(1-oxopropyl)amino]- (CA INDEX NAME)



RN 778576-40-2 ZCAPLUS

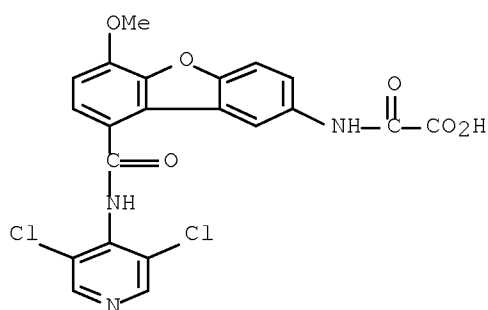
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2,2-dimethyl-1-oxopropyl)amino]-4-methoxy- (CA INDEX NAME)

10/524815



RN 778576-43-5 ZCAPLUS

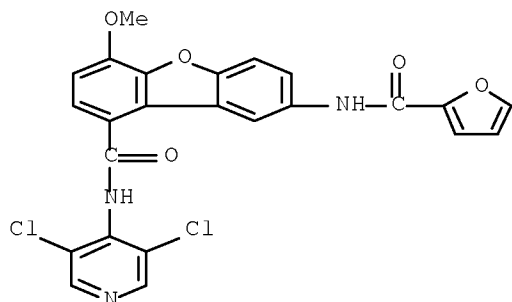
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:1) (CA INDEX NAME)



● Na

RN 778576-44-6 ZCAPLUS

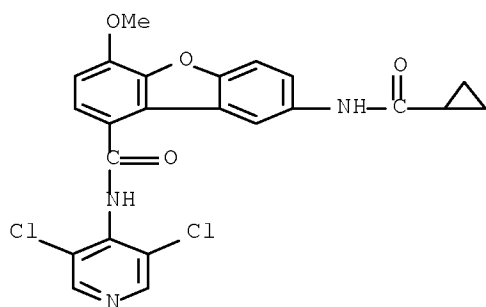
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2-furanylcarbonyl)amino]-4-methoxy- (CA INDEX NAME)



RN 778576-45-7 ZCAPLUS

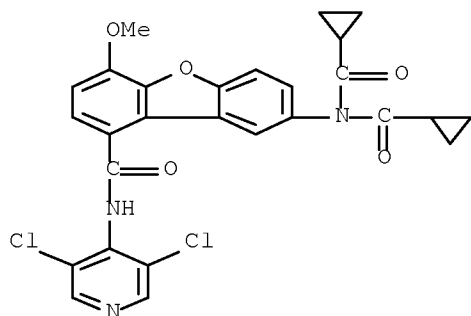
CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)

10/524815



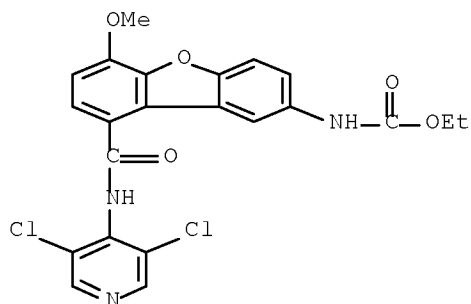
RN 778576-46-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[bis(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-47-9 ZCAPLUS

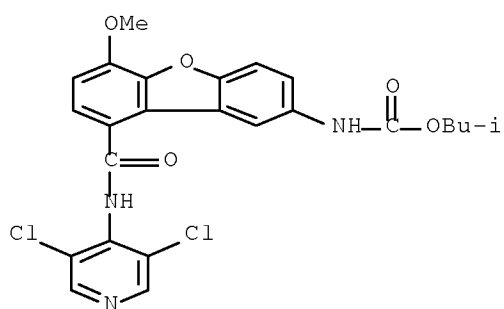
CN Carbamic acid, [9-[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 778576-48-0 ZCAPLUS

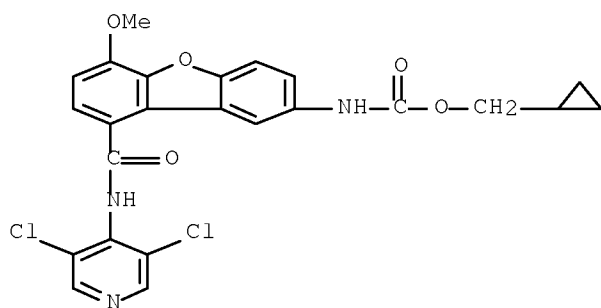
CN Carbamic acid, [9-[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

10/524815



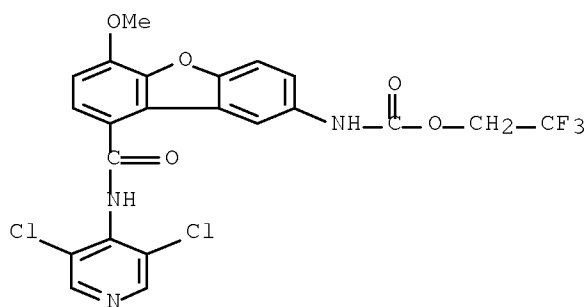
RN 778576-50-4 ZCAPLUS

CN Carbamic acid, [9-[[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, cyclopropylmethyl ester (9CI) (CA INDEX NAME)



RN 778576-51-5 ZCAPLUS

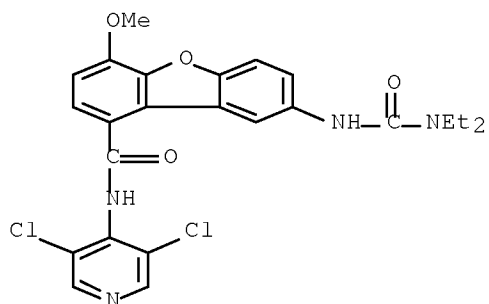
CN Carbamic acid, [9-[[[3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2,2,2-trifluoroethyl ester (9CI) (CA INDEX NAME)



RN 778576-52-6 ZCAPLUS

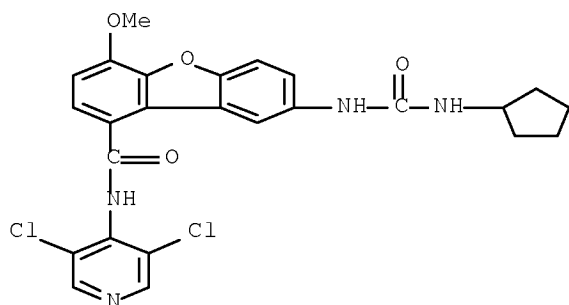
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[[(diethylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)

10/524815



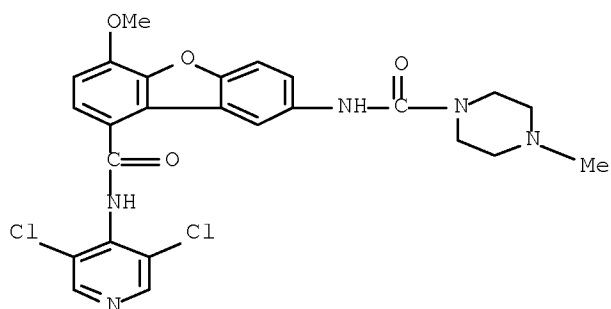
RN 778576-53-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[[[(cyclopentylamino)carbonyl]amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-55-9 ZCAPLUS

CN 1-Piperazinecarboxamide, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl-, hydrochloride (1:1) (CA INDEX NAME)

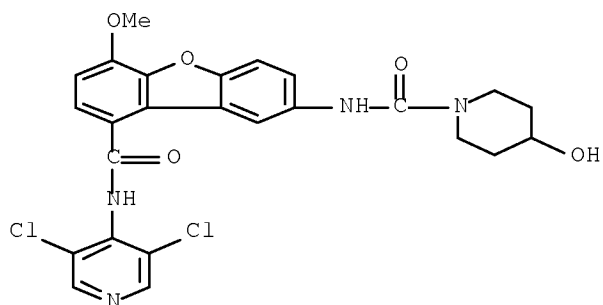


● HCl

RN 778576-56-0 ZCAPLUS

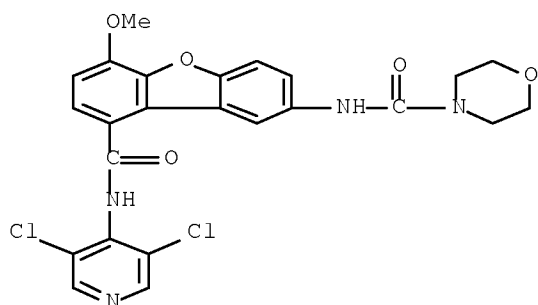
10/524815

CN 1-Piperidinecarboxamide, N-[9-[[ (3,5-dichloro-4-pyridinyl) amino] carbonyl]-6-methoxy-2-dibenzofuranyl]-4-hydroxy- (CA INDEX NAME)



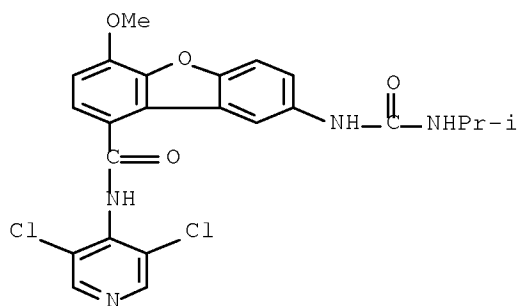
RN 778576-57-1 ZCAPLUS

CN 4-Morpholinecarboxamide, N-[9-[[ (3,5-dichloro-4-pyridinyl) amino] carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)



RN 778576-58-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[[[(1-methylethyl) amino] carbonyl] amino]- (CA INDEX NAME)



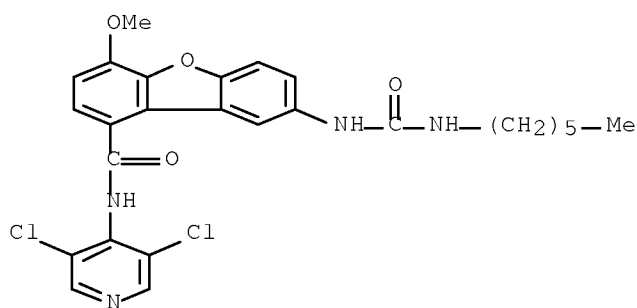
RN 778576-59-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-



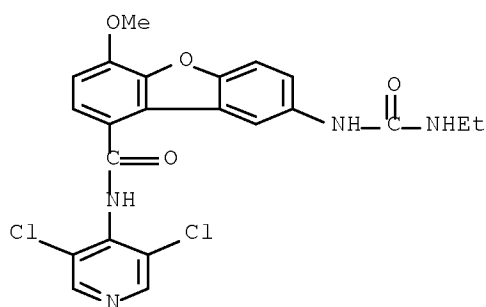
10/524815

[[ (hexylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



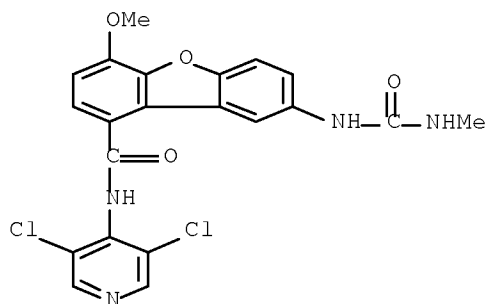
RN 778576-60-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[ (ethylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-61-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[[ (methylamino)carbonyl]amino]- (CA INDEX NAME)

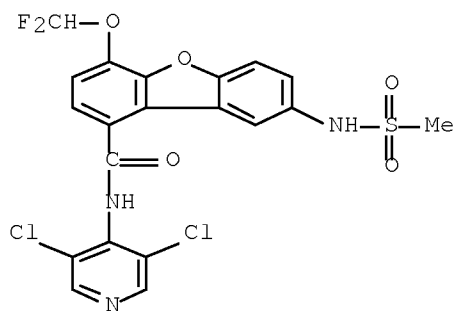


RN 778576-63-9 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:1) (CA INDEX NAME)

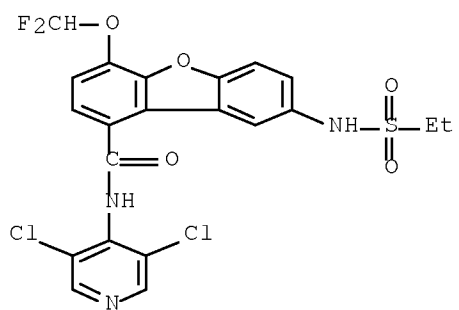
10/524815

NAME)



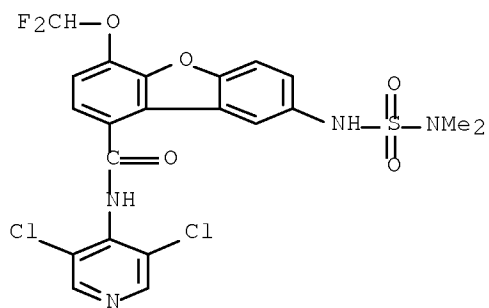
RN 778576-64-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(ethylsulfonyl)amino]- (CA INDEX NAME)



RN 778576-65-1 ZCAPLUS

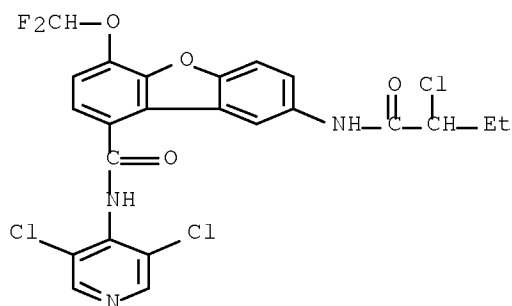
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[[ (dimethylamino)sulfonyl]amino]- (CA INDEX NAME)



10/524815

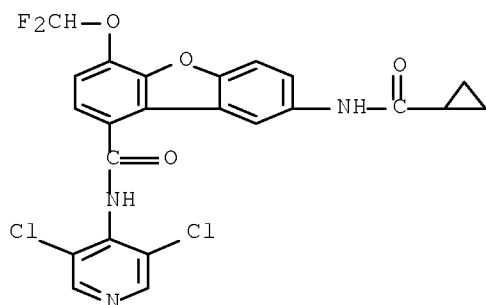
RN 778576-67-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(2-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



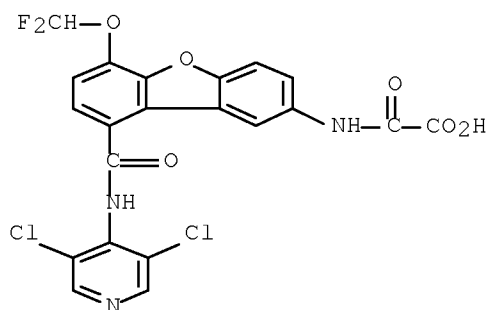
RN 778576-68-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-71-9 ZCAPLUS

CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:2) (CA INDEX NAME)

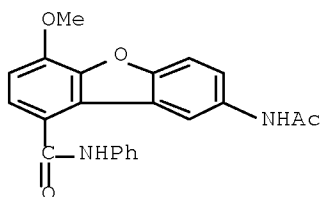


●2 Na

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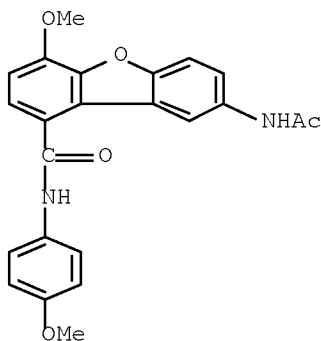
RN 778576-73-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-phenyl- (CA INDEX NAME)



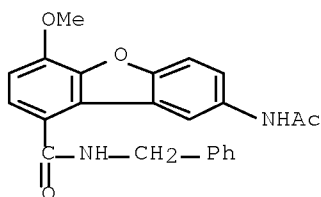
RN 778576-77-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



RN 778576-80-0 ZCAPLUS

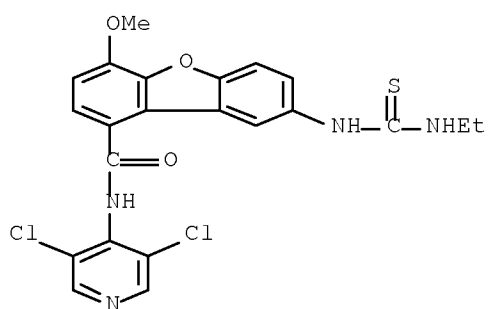
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(phenylmethyl)- (CA INDEX NAME)



RN 778576-83-3 ZCAPLUS

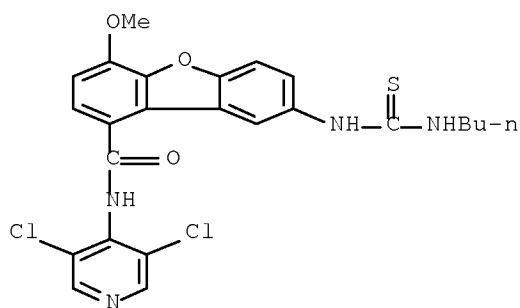
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[ (ethylamino)thioxomethyl]amino]-4-methoxy- (CA INDEX NAME)

10/524815



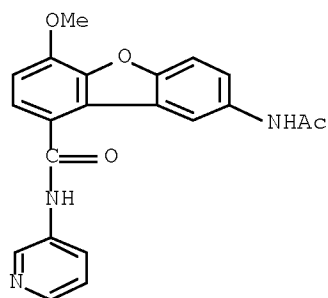
RN 778576-84-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[[[(butylamino)thioxomethyl]amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-85-5 ZCAPLUS

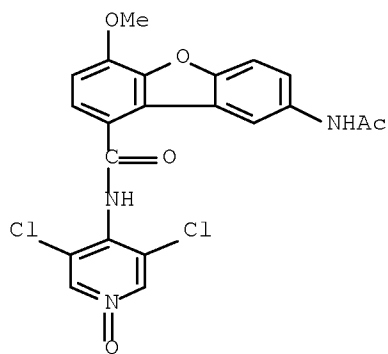
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 778576-87-7 ZCAPLUS

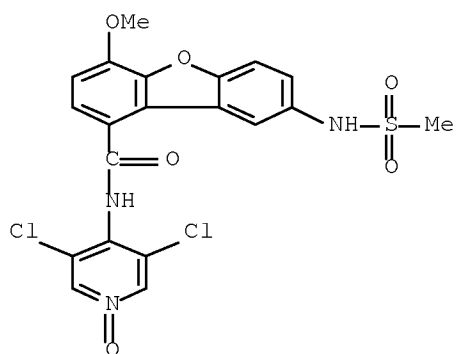
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy- (CA INDEX NAME)

10/524815



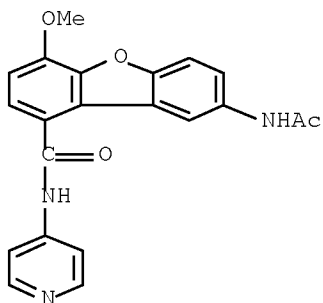
RN 778576-88-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-8-[(methylsulfonyl)amino]- (CA INDEX NAME)



RN 778576-89-9 ZCAPLUS

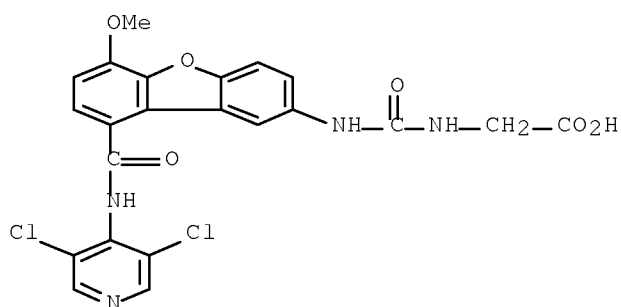
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 778576-91-3 ZCAPLUS

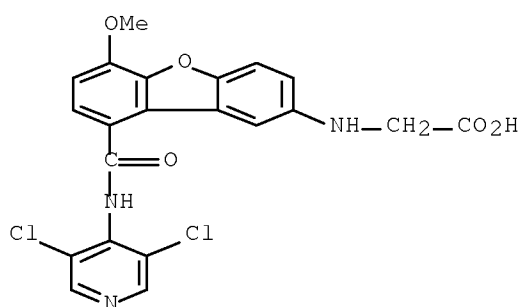
10/524815

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]- (CA INDEX NAME)



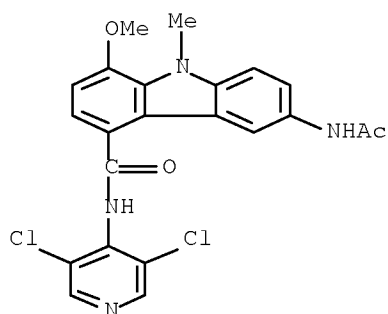
RN 778576-93-5 ZCAPLUS

CN Glycine, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)



RN 778576-94-6 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl- (CA INDEX NAME)

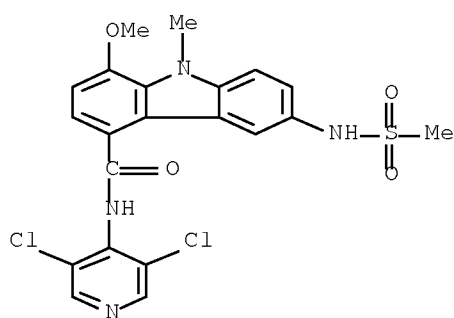


RN 778576-95-7 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-

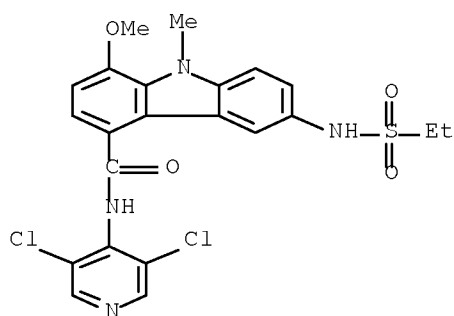
10/524815

methyl-6-[(methylsulfonyl)amino]- (CA INDEX NAME)



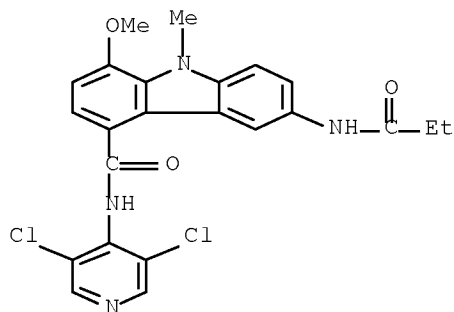
RN 778576-96-8 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-6-[(ethylsulfonyl)amino]-1-methoxy-9-methyl- (CA INDEX NAME)



RN 778576-97-9 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl-6-[(1-oxopropyl)amino]- (CA INDEX NAME)



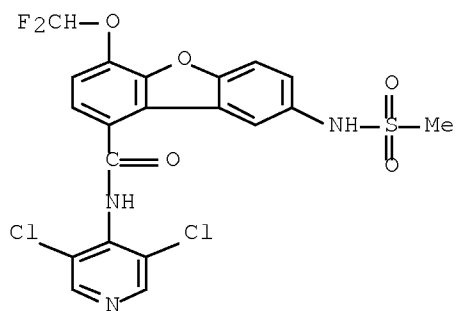
RN 778576-98-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:2) (CA INDEX NAME)



10/524815

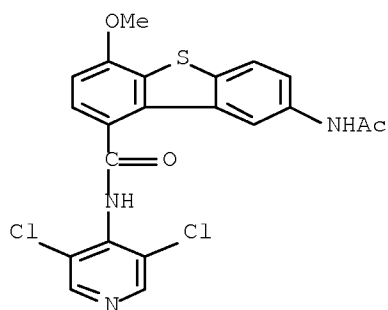
NAME)



●2 Na

RN 778576-99-1 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy-, sodium salt (1:2) (CA INDEX NAME)

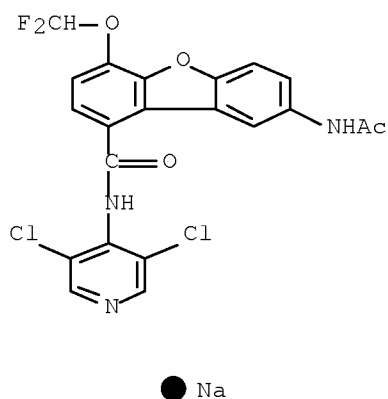


●2 Na

RN 778577-06-3 ZCAPLUS

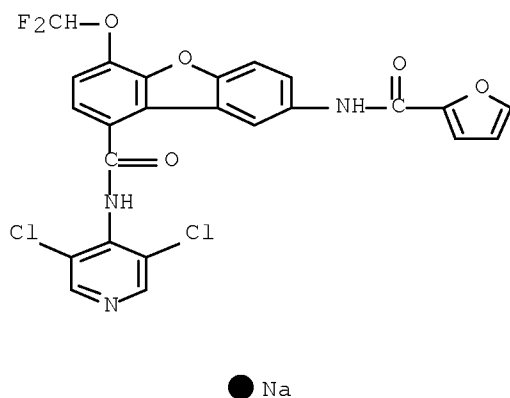
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-, sodium salt (1:1) (CA INDEX NAME)

10/524815



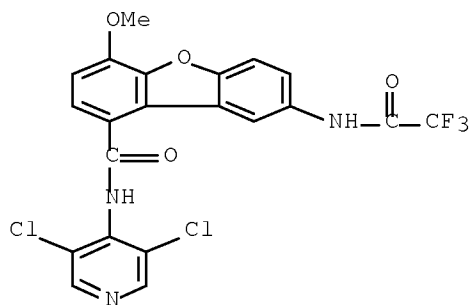
RN 778577-07-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]-, sodium salt (1:1) (CA INDEX NAME)



RN 778581-69-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[(2,2,2-trifluoroacetyl)amino]- (CA INDEX NAME)



10/524815

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD  
(7 CITINGS)  
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 4 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:675744 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:207059

TITLE: **Tricyclic** compounds (dibenzofurans, dibenzothiophenes, carbazoles, and analogs) with PDE4 inhibitory activity, useful for the treatment of inflammatory and allergic disorders, process for their preparation, and methods of use

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Bedekar, Sarika Suhas

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

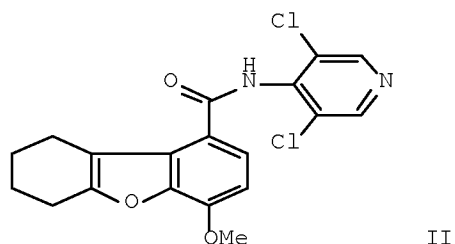
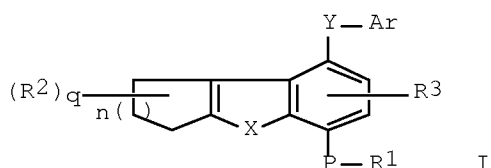
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069831	A1	20040819	WO 2004-IB330	20040210 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00177	A	20050204	IN 2003-MU177	20030210 <--
PRIORITY APPLN. INFO.:			IN 2003-MU177	A 20030210 <--
OTHER SOURCE(S):			MARPAT 141:207059	

GI



- AB The invention relates to novel heterocyclic compds. and their analogs, tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, appropriate oxides, and pharmaceutically acceptable solvates, as well as pharmaceutical compns. containing them. The invention more particularly relates to novel phosphodiesterase type 4 (PDE4) inhibitors. In particular, compds. I and their aforementioned related compds. are claimed [wherein: R1, R2, R3 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, protecting groups, or two ortho R2 may form 3- to 7-membered ring with 0-2 optional NR1/O/S heteroatoms; X = O, S(O)m, NH, or NR5; Y = CONR4, NR4SO2, SO2NR4, and NR4CO; P = O or S; q = 0-5; n = 1-3; m = 0-2; Ar = (un)substituted aryl, arylalkyl, heterocyclic, or heteroaryl; R4 = H, (un)substituted alkyl, OH, OR1, aryl, or heterocyclic; R5 = (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, and protecting groups]. The compds. (33 examples) were prepared and tested for PDE4 inhibitory activity. For instance, 6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-carboxylic acid chloride [prepared in 5 steps from 2-methoxyphenol (guaicol) and 2-bromocyclohexanone] was amidated with 4-amino-3,5-dichloropyridine in DMF/THF to give invention compound II. This compound had an IC50 value of 0.4468 nM against PDE4 in vitro.
- IC ICM C07D405-12  
ICS C07D409-12; C07D401-12; C07D307-92; A61K031-343; A61K031-381; A61K031-403
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1
- ST ~~tricyclic~~ prepn phosphodiesterase 4 inhibitor antiinflammatory antiallergic; pyridyl dibenzofuran dibenzothiophene carbazole PDE4 inhibitor inflammation allergy treatment
- IT Alzheimer's disease  
Amnesia  
Asthma  
Central nervous system, disease  
Cystic fibrosis  
Eczema  
Gout  
Immune disease  
Inflammation  
Multiple sclerosis  
Osteoarthritis  
Psoriasis  
Respiratory distress syndrome  
Rheumatoid arthritis  
Shock (circulatory collapse)  
Urticaria  
(treatment of; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)
- IT 740872-01-9P, 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
740872-02-0P, 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-03-1P,  
3-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
740872-04-2P, 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-

ylcarboxamido)fluorobenzene 740872-05-3P,  
 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine N-oxide 740872-06-4P,  
 (±)-3,5-Dichloro-4-(6-methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-07-5P, (±)-4-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-08-6P, (±)-3-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-09-7P, 3,5-Dichloro-4-(6-difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-10-0P, 4-(6-Difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-11-1P, 3-(6-Difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-12-2P, 3,5-Dichloro-4-(6-cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-13-3P, 4-(6-Cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-14-4P, 3-(6-Cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-15-5P, 3,5-Dichloro-4-(6-ethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-16-6P, 3-(6-Ethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-17-7P,  
 3,5-Dichloro-4-(6-isopropoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-18-8P,  
 3,5-Dichloro-4-(6-cyclopentyloxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-19-9P,  
 3,5-Dichloro-4-[4-methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-20-2P,  
 4-[4-Methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-21-3P,  
 3-[4-Methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-22-4P,  
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 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]thiophen-9-ylcarboxamido)pyridine 740872-24-6P,  
 N5-(4-Pyridyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-25-7P, N5-(3,5-Dichloro-4-pyridyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-26-8P,  
 N5-(4-Pyridyl)-9-cyclohexylmethyl-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-27-9P,  
 N5-(3,5-Dichloro-4-pyridyl)-9-cyclohexylmethyl-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-28-0P,  
 N5-(4-Pyridyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-29-1P,  
 N5-(4-Methoxyphenyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-30-4P,  
 N5-(3,5-Dichloro-4-pyridyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-31-5P,  
 N1-(4-Pyridyl)-4-methoxy-5,6,7,8,9,10-hexahydrocyclohepta[b]indole-1-carboxamide 740872-32-6P,  
 N1-(3,5-Dichloro-4-pyridyl)-4-methoxy-5,6,7,8,9,10-hexahydrocyclohepta[b]indole-1-carboxamide 740872-33-7P,  
 N8-(3,5-Dichloro-4-pyridyl)-5-methoxy-1,2,3,4-tetrahydrocyclopenta[b]indole-8-carboxamide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);  
 THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(drug candidate; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

IT 740872-01-9P, 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-02-0P, 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-03-1P,  
 3-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-04-2P, 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)fluorobenzene 740872-05-3P,  
 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine N-oxide 740872-06-4P,  
 (±)-3,5-Dichloro-4-(6-methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-07-5P, (±)-4-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-08-6P, (±)-3-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-09-7P, 3,5-Dichloro-4-(6-difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-10-0P, 4-(6-Difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-11-1P, 3-(6-Difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-12-2P, 3,5-Dichloro-4-(6-cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-13-3P, 4-(6-Cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-14-4P, 3-(6-Cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-15-5P, 3,5-Dichloro-4-(6-ethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine  
 740872-16-6P, 3-(6-Ethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-17-7P,  
 3,5-Dichloro-4-(6-isopropoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-18-8P,  
 3,5-Dichloro-4-(6-cyclopentyloxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-19-9P,  
 3,5-Dichloro-4-[4-methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-20-2P,  
 4-[4-Methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-21-3P,  
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 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]thiophen-9-ylcarboxamido)pyridine 740872-23-5P,  
 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]thiophen-9-ylcarboxamido)pyridine 740872-24-6P,  
 N5-(4-Pyridyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-25-7P, N5-(3,5-Dichloro-4-pyridyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-26-8P,  
 N5-(4-Pyridyl)-9-cyclohexylmethyl-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-27-9P,  
 N5-(3,5-Dichloro-4-pyridyl)-9-cyclohexylmethyl-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-28-0P,  
 N5-(4-Pyridyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-29-1P,  
 N5-(4-Methoxyphenyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-30-4P,

10/524815

N5-(3,5-Dichloro-4-pyridyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-31-5P,  
N1-(4-Pyridyl)-4-methoxy-5,6,7,8,9,10-hexahydrocyclohepta[b]indole-1-carboxamide 740872-32-6P,

N1-(3,5-Dichloro-4-pyridyl)-4-methoxy-5,6,7,8,9,10-hexahydrocyclohepta[b]indole-1-carboxamide 740872-33-7P,

N8-(3,5-Dichloro-4-pyridyl)-5-methoxy-1,2,3,4-tetrahydrocyclopenta[b]indole-8-carboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

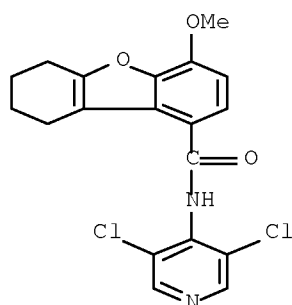
THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(drug candidate; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

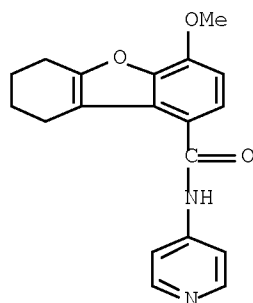
RN 740872-01-9 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro-4-methoxy- (CA INDEX NAME)



RN 740872-02-0 ZCAPLUS

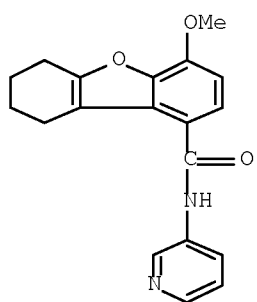
CN 1-Dibenzofurancarboxamide, 6,7,8,9-tetrahydro-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-03-1 ZCAPLUS

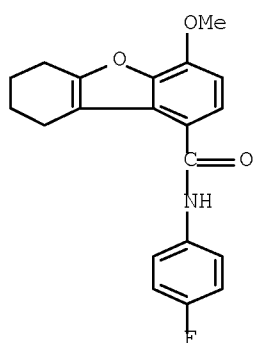
CN 1-Dibenzofurancarboxamide, 6,7,8,9-tetrahydro-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)

10/524815



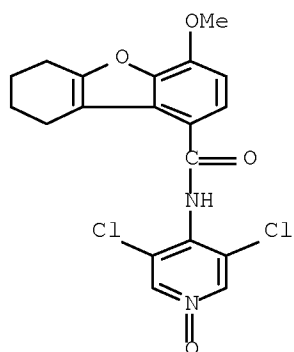
RN 740872-04-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(4-fluorophenyl)-6,7,8,9-tetrahydro-4-methoxy-  
(CA INDEX NAME)



RN 740872-05-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-6,7,8,9-  
tetrahydro-4-methoxy- (CA INDEX NAME)

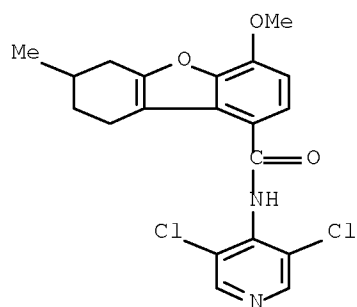


RN 740872-06-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro-  
4-methoxy-7-methyl- (CA INDEX NAME)

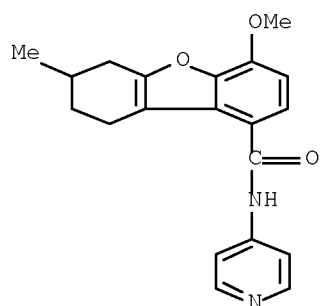


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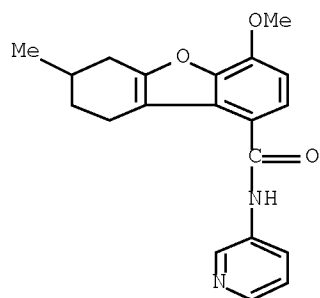
RN 740872-07-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 6,7,8,9-tetrahydro-4-methoxy-7-methyl-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-08-6 ZCAPLUS

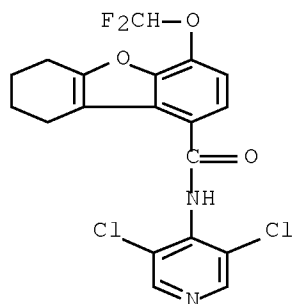
CN 1-Dibenzofurancarboxamide, 6,7,8,9-tetrahydro-4-methoxy-7-methyl-N-3-pyridinyl- (CA INDEX NAME)



RN 740872-09-7 ZCAPLUS

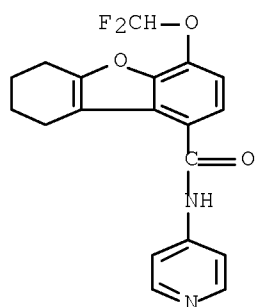
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-6,7,8,9-tetrahydro- (CA INDEX NAME)

10/524815



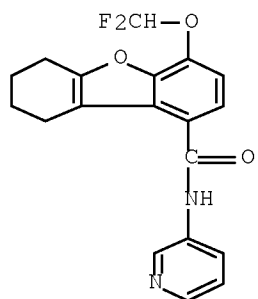
RN 740872-10-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-6,7,8,9-tetrahydro-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-11-1 ZCAPLUS

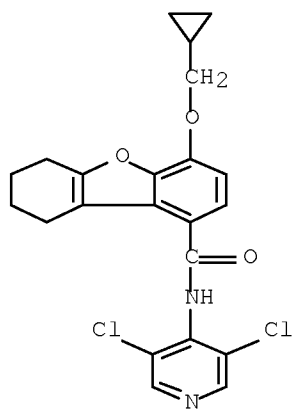
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-6,7,8,9-tetrahydro-N-3-pyridinyl- (CA INDEX NAME)



RN 740872-12-2 ZCAPLUS

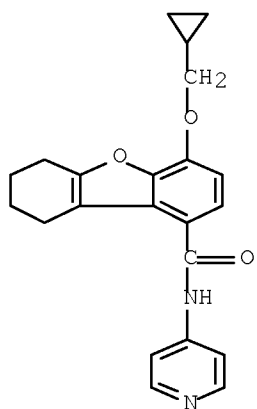
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)

10/524815



RN 740872-13-3 ZCAPLUS

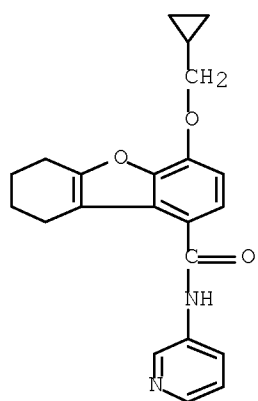
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-6,7,8,9-tetrahydro-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-14-4 ZCAPLUS

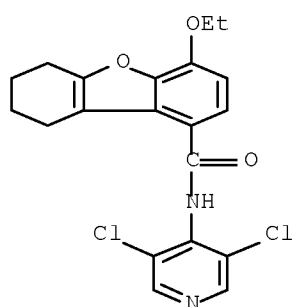
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-6,7,8,9-tetrahydro-N-3-pyridinyl- (CA INDEX NAME)

10/524815



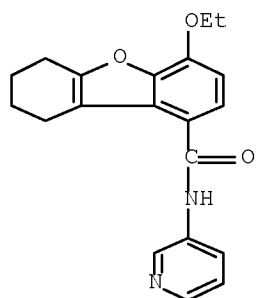
RN 740872-15-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-ethoxy-6,7,8,9-tetrahydro- (CA INDEX NAME)



RN 740872-16-6 ZCAPLUS

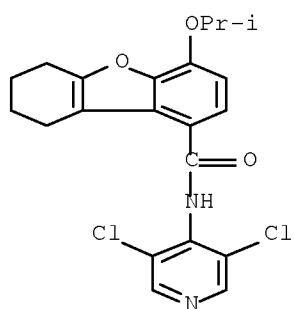
CN 1-Dibenzofurancarboxamide, 4-ethoxy-6,7,8,9-tetrahydro-N-3-pyridinyl- (CA INDEX NAME)



RN 740872-17-7 ZCAPLUS

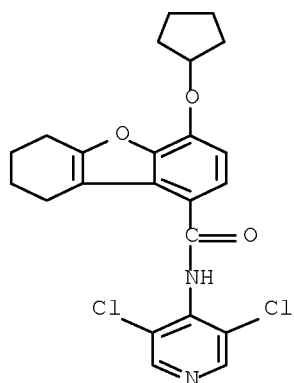
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro-4-(1-methylethoxy)- (CA INDEX NAME)

10/524815



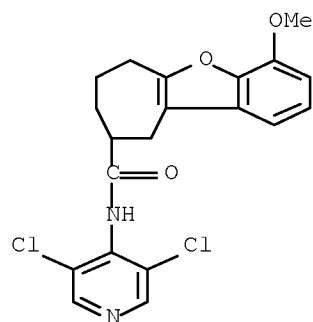
RN 740872-18-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopentyloxy)-N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)



RN 740872-19-9 ZCAPLUS

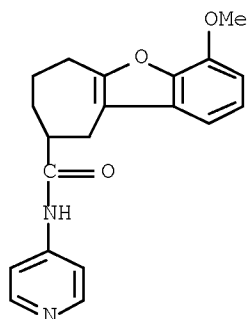
CN 6H-Benzo[b]cyclohepta[d]furan-9-carboxamide, N-(3,5-dichloro-4-pyridinyl)-7,8,9,10-tetrahydro-4-methoxy- (CA INDEX NAME)



10/524815

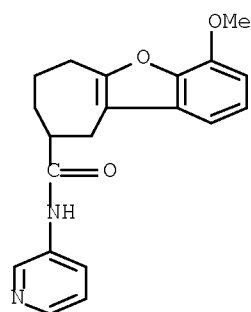
RN 740872-20-2 ZCAPLUS

CN 6H-Benzo[b]cyclohepta[d]furan-9-carboxamide,  
7,8,9,10-tetrahydro-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



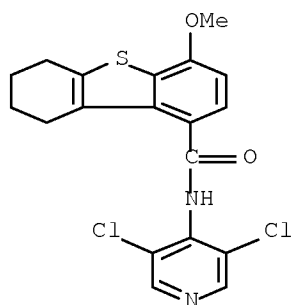
RN 740872-21-3 ZCAPLUS

CN 6H-Benzo[b]cyclohepta[d]furan-9-carboxamide,  
7,8,9,10-tetrahydro-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 740872-22-4 ZCAPLUS

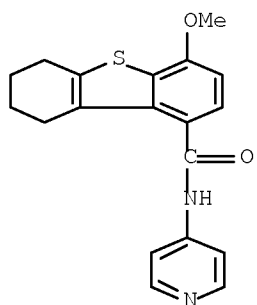
CN 1-Dibenzothiophenecarboxamide, N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro-4-methoxy- (CA INDEX NAME)



10/524815

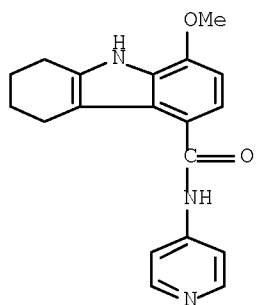
RN 740872-23-5 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, 6,7,8,9-tetrahydro-4-methoxy-N-4-pyridinyl-  
(CA INDEX NAME)



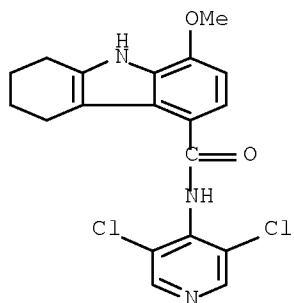
RN 740872-24-6 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 2,3,4,9-tetrahydro-8-methoxy-N-4-pyridinyl-  
(CA INDEX NAME)



RN 740872-25-7 ZCAPLUS

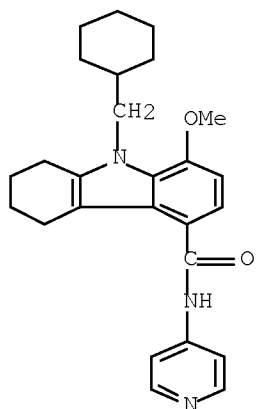
CN 1H-Carbazole-5-carboxamide, N-(3,5-dichloro-4-pyridinyl)-2,3,4,9-tetrahydro-8-methoxy- (CA INDEX NAME)



10/524815

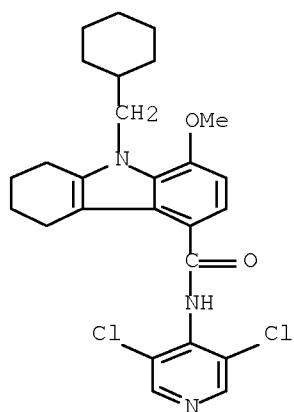
RN 740872-26-8 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 9-(cyclohexylmethyl)-2,3,4,9-tetrahydro-8-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-27-9 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 9-(cyclohexylmethyl)-N-(3,5-dichloro-4-pyridinyl)-2,3,4,9-tetrahydro-8-methoxy- (CA INDEX NAME)

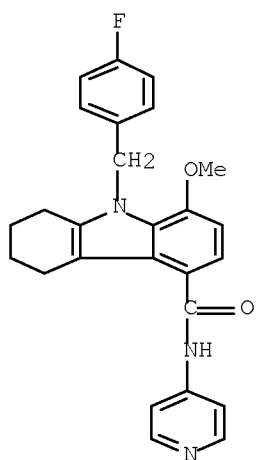


RN 740872-28-0 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 9-[(4-fluorophenyl)methyl]-2,3,4,9-tetrahydro-8-methoxy-N-4-pyridinyl- (CA INDEX NAME)



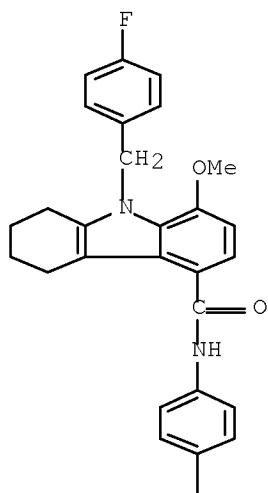
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RN 740872-29-1 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 9-[(4-fluorophenyl)methyl]-2,3,4,9-tetrahydro-8-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)

PAGE 1-A



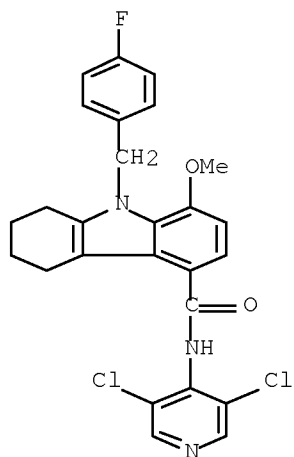
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RN 740872-30-4 ZCAPLUS

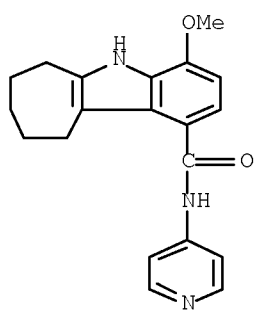
CN 1H-Carbazole-5-carboxamide, N-(3,5-dichloro-4-pyridinyl)-9-[(4-fluorophenyl)methyl]-2,3,4,9-tetrahydro-8-methoxy- (CA INDEX NAME)

10/524815



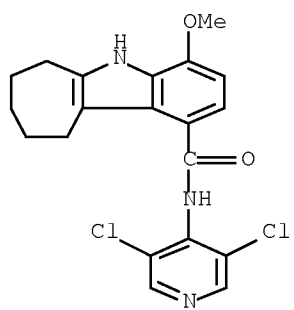
RN 740872-31-5 ZCAPLUS

CN Cyclohept[b]indole-1-carboxamide, 5,6,7,8,9,10-hexahydro-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



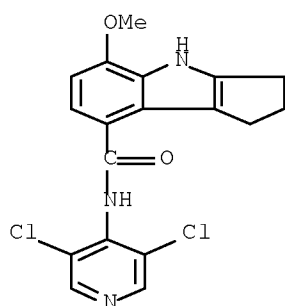
RN 740872-32-6 ZCAPLUS

CN Cyclohept[b]indole-1-carboxamide, N-(3,5-dichloro-4-pyridinyl)-5,6,7,8,9,10-hexahydro-4-methoxy- (CA INDEX NAME)



10/524815

RN 740872-33-7 ZCAPLUS  
 CN Cyclopent[b]indole-8-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,2,3,4-tetrahydro-5-methoxy- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)  
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 5 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2004:370918 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 140:391192  
 TITLE: Preparation of dibenzofuran/dibenzothiophene derivatives useful for the treatment of inflammatory and allergic disorders  
 INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram  
 PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India  
 SOURCE: PCT Int. Appl., 254 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037805	A1	20040506	WO 2003-IB4442	20031008 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2002MU00922	A	20050304	IN 2002-MU922	20021023 <--
CA 2503015	A1	20040506	CA 2003-2503015	20031008 <--
AU 2003269317	A1	20040513	AU 2003-269317	20031008 <--
EP 1554262	A1	20050720	EP 2003-751096	20031008 <--
EP 1554262	B1	20071205		
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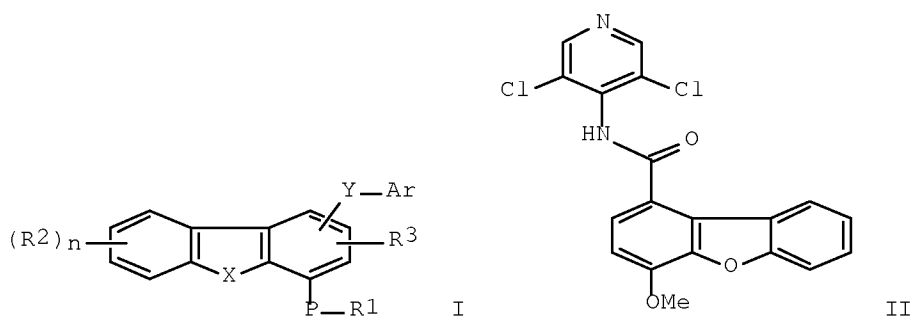
10/524815

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003014721	A	20050802	BR 2003-14721	20031008 <--
CN 1729181	A	20060201	CN 2003-80107246	20031008 <--
JP 2006506379	T	20060223	JP 2004-546246	20031008 <--
AT 380185	T	20071215	AT 2003-751096	20031008 <--
ES 2298552	T3	20080516	ES 2003-751096	20031008 <--
ZA 2005002969	A	20060222	ZA 2005-2969	20050413 <--
US 20060178418	A1	20060810	US 2005-532273	20050926 <--
US 7238725	B2	20070703		
US 20080146810	A1	20080619	US 2007-769074	20070627 <--
PRIORITY APPLN. INFO.:			IN 2002-MU922	A 20021023 <--
			WO 2003-IB4442	W 20031008 <--
			US 2005-532273	A1 20050926

OTHER SOURCE(S):           MARPAT 140:391192

GI



AB Title compds. I [R1-3 = H, alk(en/yn)yl, cycloalkyl, etc.; P = O, S; n = 0-4; Ar = (un)substituted aryl, etc.; Y = carboxamido, aminosulfonyl, etc.] are prepared For instance, 4-methoxydibenzofuran-1-carboxylic acid (preparation given) is converted to the corresponding acid chloride (PhH, SOCl<sub>2</sub>, reflux, 4 h) and treated with 4-amino-3,5-dichloropyridine (DMF/THF, NaH, -10°) to give II. II has IC<sub>50</sub> = 0.8 nM for PDE4. I are useful for the treatment of inflammatory conditions, diseases of the central nervous and insulin resistant diabetes.

IC ICM C07D307-91  
ICS C07D333-76; C07D209-88; C07D405-12; C07D401-12; C07D409-12; C07D405-14; A61K031-403; A61K031-34; A61K031-381; A61P037-00; A61P025-00; A61P003-10

CC 27-9 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1, 63

ST tricyclic dibenzofuran dibenzothiophene inflammatory allergic process  
prepn

IT Alzheimer's disease  
Amnesia  
Anti-inflammatory agents  
Antiarthritics  
Antiasthmatics  
Antidepressants  
Antidiabetic agents  
Antirheumatic agents  
Asthma  
Cystic fibrosis  
Diabetes insipidus

Diabetes mellitus

Gout

Human

Immune disease

Inflammation

Multiple sclerosis

Nervous system agents

Osteoarthritis

Psoriasis

Respiratory distress syndrome

Rheumatoid arthritis

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

IT 685874-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide 685874-44-6P,  
N-(Pyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide  
685874-48-0P, N-(Pyridin-3-yl)-4-methoxydibenzofuran-1-carboxamide  
685874-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-trifluoromethyldibenzofuran-1-carboxamide 685874-53-7P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-trifluoromethyldibenzofuran-1-carboxamide 685874-55-9P,  
N-(Pyridin-4-yl)-4-difluoromethoxy-8-trifluoromethyldibenzofuran-1-carboxamide 685874-57-1P,  
N-(Pyridin-3-yl)-4-difluoromethoxy-8-trifluoromethyldibenzofuran-1-carboxamide 685874-60-6P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685874-61-7P, N-(Pyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685874-63-9P,  
N-(Pyridin-3-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685874-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide 685874-68-4P,  
N-(Pyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide 685874-70-8P, N-(Pyridin-3-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide 685874-72-0P,  
N-(3,5-Dichloropyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide 685874-74-2P, N-(Pyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide 685874-76-4P,  
N-(Pyridin-3-yl)-4-isopropoxydibenzofuran-1-carboxamide 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-nitrodibenzofuran-1-carboxamide 685875-02-9P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzofuran-1-carboxamide 685875-03-0P,  
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzofuran-1-carboxamide 685875-04-1P,  
3,5-Dichloro-4-(4-ethoxydibenzofuran-1-ylcarboxamido)pyridine 685875-07-4P, 3,5-Dichloro-4-(4-cyclopentyloxydibenzofuran-1-ylcarboxamido)pyridine 685875-14-3P,  
N-Formyl-1-methoxy-4-(((4-methoxyphenyl)amino)sulfonyl)-9H-carbazole 685875-16-5P, N-Formyl-1-methoxy-4-(((4-methylphenyl)amino)sulfonyl)-9H-carbazole 685875-17-6P,  
1-Methoxy-4-(((4-methylphenyl)amino)sulfonyl)-9H-carbazole 685875-18-7P 685875-78-9P 685875-79-0P  
685875-80-3P, N-(4-Methoxyphenyl)-4-methoxydibenzothiophene-1-carboxamide 685875-97-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

IT 685874-43-5P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-

methoxydibenzofuran-1-carboxamide 685874-45-7P,  
 N-(1-Oxopyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide  
 685874-46-8P, N-(2-Chloropyridin-3-yl)-4-methoxydibenzofuran-1-  
 carboxamide 685874-47-9P,  
 N-(4-Fluorophenyl)-4-methoxydibenzofuran-1-carboxamide  
 685874-49-1P, N-(1-Oxopyridin-3-yl)-4-methoxydibenzofuran-1-  
 carboxamide 685874-51-5P,  
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-  
 1-carboxamide 685874-52-6P,  
 N-(Pyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-1-carboxamide  
 685874-54-8P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxy-  
 8-trifluoromethylidibenzofuran-1-carboxamide 685874-56-0P,  
 N-(1-Oxopyridin-4-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-  
 carboxamide 685874-58-2P,  
 N-(1-Oxopyridin-3-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-  
 carboxamide 685874-59-3P,  
 N-(Pyridin-2-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-  
 carboxamide 685874-62-8P,  
 N-(1-Oxopyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide  
 685874-64-0P, N-(1-Oxopyridin-3-yl)-4-difluoromethoxydibenzofuran-  
 1-carboxamide 685874-65-1P,  
 N-(5-Chloropyridin-2-yl)-4-difluoromethoxydibenzofuran-1-carboxamide  
 685874-67-3P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-  
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 N-(1-Oxopyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide  
 685874-71-9P, N-(1-Oxopyridin-3-yl)-4-  
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 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-isopropoxydibenzofuran-1-  
 carboxamide 685874-75-3P,  
 N-(1-Oxopyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide  
 685874-77-5P, N-(1-Oxopyridin-3-yl)-4-isopropoxydibenzofuran-1-  
 carboxamide 685874-78-6P,  
 N-(3,5-Dichloropyridin-4-yl)-4-benzyloxydibenzofuran-1-carboxamide  
 685874-80-0P, N-(Pyridin-4-yl)-4-methoxy-8-nitrodibenzofuran-1-  
 carboxamide 685874-81-1P,  
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzofuran-1-carboxamide  
 685874-82-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
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 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-bromodibenzofuran-1-carboxamide  
 685874-84-4P, N-(Pyridin-4-yl)-4-methoxy-8-bromodibenzofuran-1-  
 carboxamide 685874-85-5P,  
 N-(Pyridin-3-yl)-4-methoxy-8-bromodibenzofuran-1-carboxamide  
 685874-86-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
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 685874-88-8P, N-(Pyridin-3-yl)-4-methoxy-8-iododibenzofuran-1-  
 carboxamide 685874-89-9P,  
 N-(4-Methylpyrimidin-2-yl)-4-methoxydibenzofuran-1-carboxamide  
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 carboxamide 685874-91-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-ethoxycarbomethoxydibenzofuran-1-  
 carboxamide 685874-92-4P,  
 N-(3,5-Dichloropyridin-4-yl)-4-[(carboxy)methoxy]dibenzofuran-1-  
 carboxamide 685874-93-5P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-2-carboxamide  
 685874-94-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-3-  
 carboxamide 685874-95-7P 685874-96-8P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-1-sulfonamide  
 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 aminodibenzofuran-1-carboxamide 685874-99-1P,

N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685875-00-7P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-cyanodibenzofuran-1-carboxamide 685875-05-2P, N-Benzyl-4-cyclopentyloxydibenzofuran-1-carboxamide 685875-06-3P, 4-[4-[(Cyclopentyl)oxy]dibenzofuran-1-ylcarboxamido]pyridine 685875-08-5P,  
 4-(4-Methylsulfanyldibenzofuran-1-ylcarboxamido)pyridine 685875-09-6P, N-(4-Methoxydibenzofuran-1-yl)nicotinamide 685875-10-9P, N-Benzyl-4-methoxydibenzofuran-1-sulfonamide 685875-11-0P, 4-(((4-Methoxydibenzofuran-1-yl)sulfonyl)amino)pyridine 685875-12-1P 685875-13-2P  
 685875-15-4P, 1-Methoxy-4-(((4-methoxyphenyl)amino)sulfonyl)-9H-carbazole 685875-20-1P 685875-21-2P,  
 1-Methoxy-4-[[ (pyridin-4-yl)amino]sulfonyl]-9H-carbazole 685875-22-3P, N-(2,6-Dichlorophenyl)-1-methoxy-9H-4-carbazolsulfonamide 685875-23-4P,  
 N-(2,6-Dichlorophenyl)-9-formyl-1-methoxy-9H-4-carbazolsulfonamide 685875-24-5P, N-(Pyridin-4-yl)-1-methoxy-9H-4-carbazolecarboxamide 685875-25-6P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9H-4-carbazolecarboxamide 685875-26-7P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-1-methoxy-9H-4-carbazolecarboxamide 685875-30-3P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-6-chloro-1-methoxy-9H-4-carbazolecarboxamide 685875-32-5P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-carbazolecarboxamide 685875-34-7P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-36-9P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-methoxybenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-38-1P,  
 N-(3,5-Dichloropyridin-4-yl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-41-6P,  
 N-(4-Pyridyl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-44-9P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-1-methoxy-9H-4-carbazolecarboxamide 685875-48-3P,  
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 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-72-3P,  
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-(4-methoxybenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-73-4P,  
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 N-(3,5-Dichloropyridin-4-yl)-9-methyl-1-methoxy-9H-4-carbazolecarboxamide 685875-81-4P 685875-82-5P,  
 N-(4-Chlorophenyl)-4-methoxydibenzothiophene-1-carboxamide 685875-83-6P 685875-84-7P 685875-85-8P  
 685875-86-9P 685875-87-0P 685875-89-2P  
 685875-90-5P 685875-92-7P 685875-93-8P

685875-94-9P 685875-98-3P 685875-99-4P

685876-00-0P 685876-01-1P 685876-02-2P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-(2-oxopyrrolidin-1-yl)dibenzofuran-1-carboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

IT 685874-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide 685874-44-6P,

N-(Pyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide

685874-48-0P, N-(Pyridin-3-yl)-4-methoxydibenzofuran-1-carboxamide

685874-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

trifluoromethyldibenzofuran-1-carboxamide 685874-53-7P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-

trifluoromethyldibenzofuran-1-carboxamide 685874-55-9P,

N-(Pyridin-4-yl)-4-difluoromethoxy-8-trifluoromethyldibenzofuran-1-carboxamide 685874-57-1P,

N-(Pyridin-3-yl)-4-difluoromethoxy-8-trifluoromethyldibenzofuran-1-carboxamide 685874-60-6P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide

685874-61-7P, N-(Pyridin-4-yl)-4-difluoromethoxydibenzofuran-1-

carboxamide 685874-63-9P,

N-(Pyridin-3-yl)-4-difluoromethoxydibenzofuran-1-carboxamide

685874-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-

cyclopropylmethoxydibenzofuran-1-carboxamide 685874-68-4P,

N-(Pyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide

685874-70-8P, N-(Pyridin-3-yl)-4-cyclopropylmethoxydibenzofuran-1-

carboxamide 685874-72-0P,

N-(3,5-Dichloropyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide

685874-74-2P, N-(Pyridin-4-yl)-4-isopropoxydibenzofuran-1-

carboxamide 685874-76-4P,

N-(Pyridin-3-yl)-4-isopropoxydibenzofuran-1-carboxamide

685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

nitrodibenzofuran-1-carboxamide 685875-02-9P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzofuran-1-carboxamide 685875-03-0P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzofuran-1-carboxamide 685875-04-1P,

3,5-Dichloro-4-(4-ethoxydibenzofuran-1-ylcarboxamido)pyridine

685875-07-4P, 3,5-Dichloro-4-(4-cyclopentyloxydibenzofuran-1-

ylcarboxamido)pyridine 685875-14-3P,

N-Formyl-1-methoxy-4-(((4-methoxyphenyl)amino)sulfonyl)-9H-carbazole

685875-16-5P, N-Formyl-1-methoxy-4-(((4-

methylphenyl)amino)sulfonyl)-9H-carbazole 685875-17-6P,

1-Methoxy-4-(((4-methylphenyl)amino)sulfonyl)-9H-carbazole

685875-18-7P 685875-78-9P 685875-79-0P

685875-80-3P, N-(4-Methoxyphenyl)-4-methoxydibenzothiophene-1-

carboxamide 685875-97-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

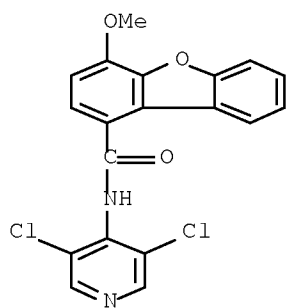
(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

RN 685874-42-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)

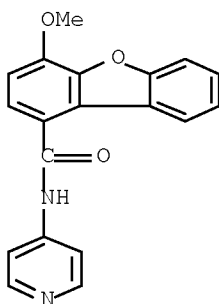


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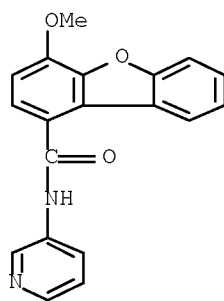
RN 685874-44-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 685874-48-0 ZCAPLUS

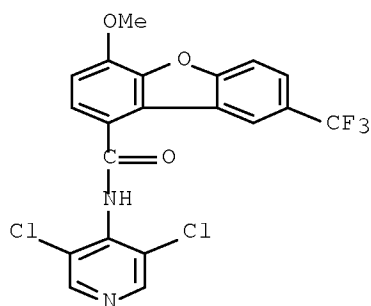
CN 1-Dibenzofurancarboxamide, 4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 685874-50-4 ZCAPLUS

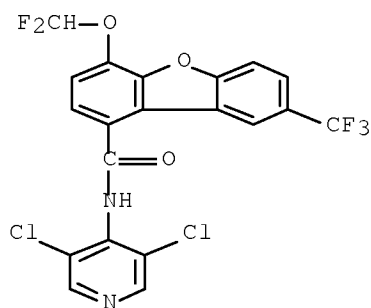
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-(trifluoromethyl)- (CA INDEX NAME)

10/524815



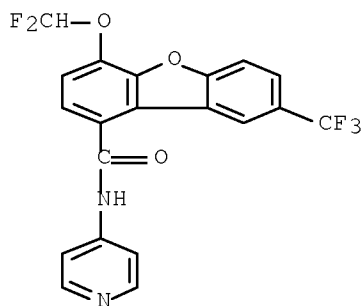
RN 685874-53-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-(trifluoromethyl)- (CA INDEX NAME)



RN 685874-55-9 ZCAPLUS

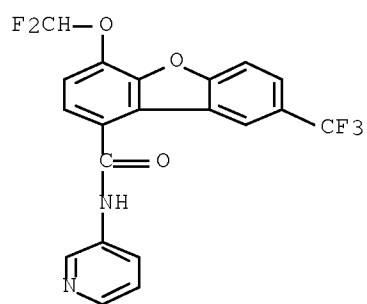
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-4-pyridinyl-8-(trifluoromethyl)- (CA INDEX NAME)



RN 685874-57-1 ZCAPLUS

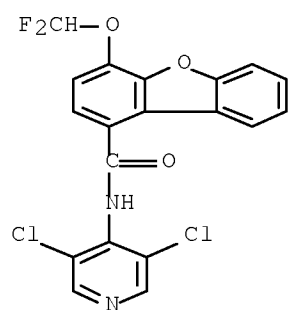
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-3-pyridinyl-8-(trifluoromethyl)- (CA INDEX NAME)

10/524815



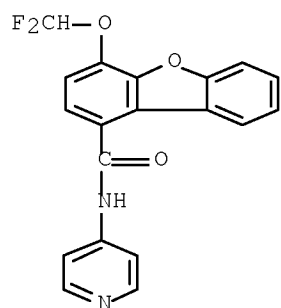
RN 685874-60-6 ZCAPLUS

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RN 685874-61-7 ZCAPLUS

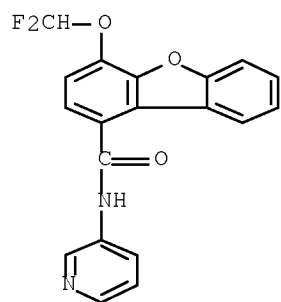
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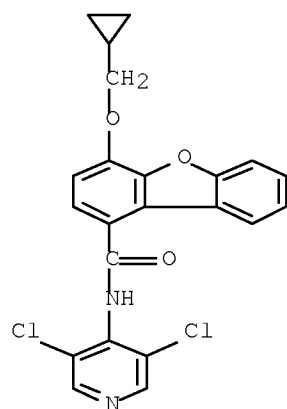
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-3-pyridinyl- (CA INDEX NAME)

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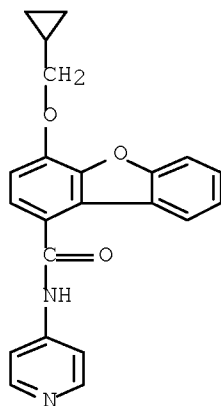
RN 685874-66-2 ZCAPLUS

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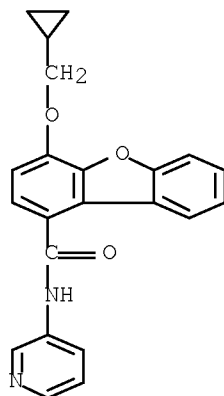
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-4-pyridinyl- (CA INDEX NAME)



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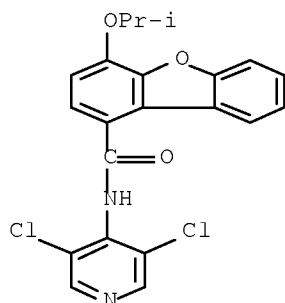
RN 685874-70-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-3-pyridinyl- (CA INDEX NAME)



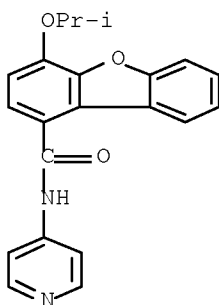
RN 685874-72-0 ZCAPLUS

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RN 685874-74-2 ZCAPLUS

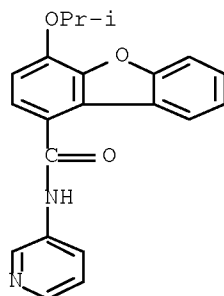
CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-4-pyridinyl- (CA INDEX NAME)



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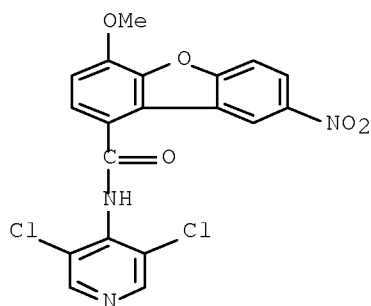
RN 685874-76-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-3-pyridinyl- (CA INDEX NAME)



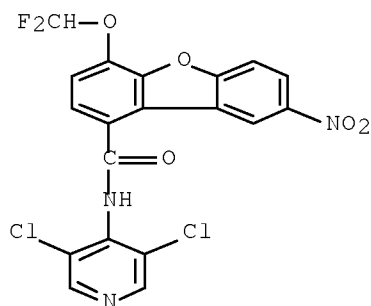
RN 685874-79-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-nitro- (CA INDEX NAME)



RN 685875-02-9 ZCAPLUS

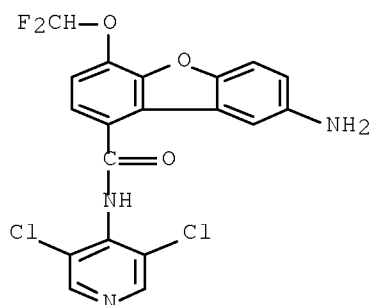
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-nitro- (CA INDEX NAME)



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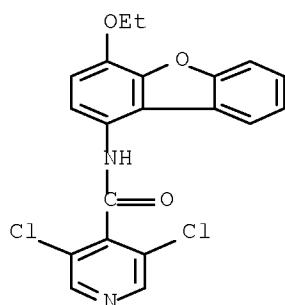
RN 685875-03-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-amino-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



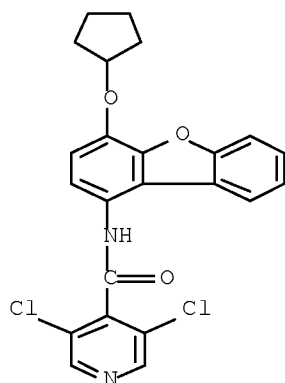
RN 685875-04-1 ZCAPLUS

CN 4-Pyridinecarboxamide, 3,5-dichloro-N-(4-ethoxy-1-dibenzofuranyl)- (CA INDEX NAME)



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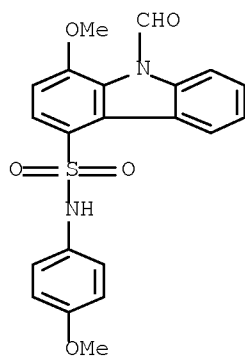
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-[4-(cyclopentyloxy)-1-dibenzofuranyl]- (CA INDEX NAME)



10/524815

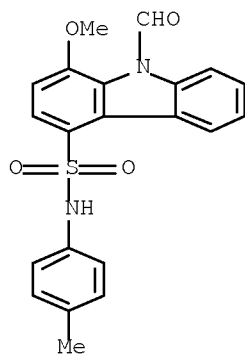
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CN 9H-Carbazole-4-sulfonamide, 9-formyl-1-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



RN 685875-16-5 ZCAPLUS

CN 9H-Carbazole-4-sulfonamide, 9-formyl-1-methoxy-N-(4-methylphenyl)- (CA INDEX NAME)

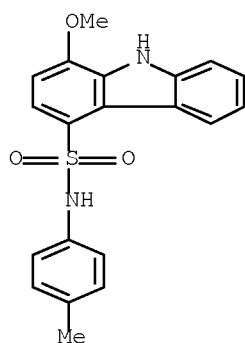


RN 685875-17-6 ZCAPLUS

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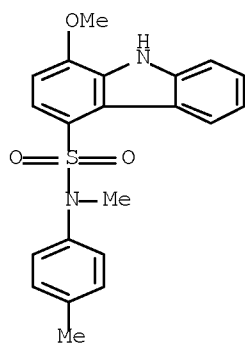


10/524815



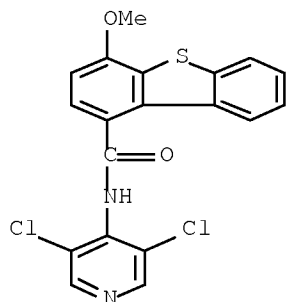
RN 685875-18-7 ZCAPLUS

CN 9H-Carbazole-4-sulfonamide, 1-methoxy-N-methyl-N-(4-methylphenyl)- (CA INDEX NAME)



RN 685875-78-9 ZCAPLUS

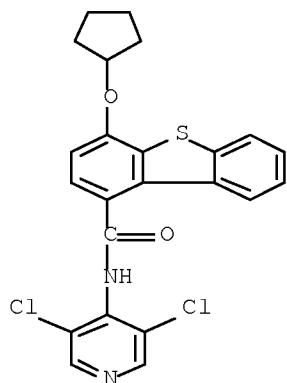
CN 1-Dibenzothiophenecarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 685875-79-0 ZCAPLUS

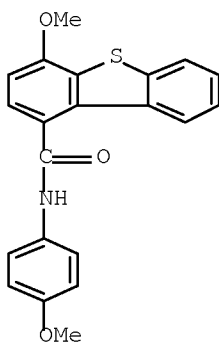
CN 1-Dibenzothiophenecarboxamide, 4-(cyclopentyloxy)-N-(3,5-dichloro-4-pyridinyl)- (CA INDEX NAME)

10/524815



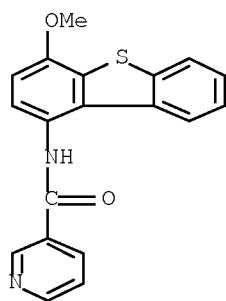
RN 685875-80-3 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, 4-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



RN 685875-97-2 ZCAPLUS

CN 3-Pyridinecarboxamide, N-(4-methoxy-1-dibenzothiophen-2-yl)- (CA INDEX NAME)



IT 685874-43-5P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide 685874-45-7P,

N-(1-Oxopyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide  
 685874-46-8P, N-(2-Chloropyridin-3-yl)-4-methoxydibenzofuran-1-  
 carboxamide 685874-47-9P,  
 N-(4-Fluorophenyl)-4-methoxydibenzofuran-1-carboxamide  
 685874-49-1P, N-(1-Oxopyridin-3-yl)-4-methoxydibenzofuran-1-  
 carboxamide 685874-51-5P,  
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-  
 1-carboxamide 685874-52-6P,  
 N-(Pyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-1-carboxamide  
 685874-54-8P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxy-  
 8-trifluoromethylidibenzofuran-1-carboxamide 685874-56-0P,  
 N-(1-Oxopyridin-4-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-  
 carboxamide 685874-58-2P,  
 N-(1-Oxopyridin-3-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-  
 carboxamide 685874-59-3P,  
 N-(Pyridin-2-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-  
 carboxamide 685874-62-8P,  
 N-(1-Oxopyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide  
 685874-64-0P, N-(1-Oxopyridin-3-yl)-4-difluoromethoxydibenzofuran-  
 1-carboxamide 685874-65-1P,  
 N-(5-Chloropyridin-2-yl)-4-difluoromethoxydibenzofuran-1-carboxamide  
 685874-67-3P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-  
 cyclopropylmethoxydibenzofuran-1-carboxamide 685874-69-5P,  
 N-(1-Oxopyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide  
 685874-71-9P, N-(1-Oxopyridin-3-yl)-4-  
 cyclopropylmethoxydibenzofuran-1-carboxamide 685874-73-1P,  
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-isopropoxydibenzofuran-1-  
 carboxamide 685874-75-3P,  
 N-(1-Oxopyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide  
 685874-77-5P, N-(1-Oxopyridin-3-yl)-4-isopropoxydibenzofuran-1-  
 carboxamide 685874-78-6P,  
 N-(3,5-Dichloropyridin-4-yl)-4-benzyloxydibenzofuran-1-carboxamide  
 685874-80-0P, N-(Pyridin-4-yl)-4-methoxy-8-nitrodibenzofuran-1-  
 carboxamide 685874-81-1P,  
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzofuran-1-carboxamide  
 685874-82-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 chlorodibenzofuran-1-carboxamide 685874-83-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-bromodibenzofuran-1-carboxamide  
 685874-84-4P, N-(Pyridin-4-yl)-4-methoxy-8-bromodibenzofuran-1-  
 carboxamide 685874-85-5P,  
 N-(Pyridin-3-yl)-4-methoxy-8-bromodibenzofuran-1-carboxamide  
 685874-86-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 iododibenzofuran-1-carboxamide 685874-87-7P,  
 N-(Pyridin-4-yl)-4-methoxy-8-iododibenzofuran-1-carboxamide  
 685874-88-8P, N-(Pyridin-3-yl)-4-methoxy-8-iododibenzofuran-1-  
 carboxamide 685874-89-9P,  
 N-(4-Methylpyrimidin-2-yl)-4-methoxydibenzofuran-1-carboxamide  
 685874-90-2P, N-(2,5-Dichlorophenyl)-4-methoxydibenzofuran-1-  
 carboxamide 685874-91-3P,  
 N-(3,5-Dichloropyridin-4-yl)-4-ethoxycarbomethoxydibenzofuran-1-  
 carboxamide 685874-92-4P,  
 N-(3,5-Dichloropyridin-4-yl)-4-[(carboxy)methoxy]dibenzofuran-1-  
 carboxamide 685874-93-5P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-2-carboxamide  
 685874-94-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-3-  
 carboxamide 685874-95-7P 685874-96-8P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-1-sulfonamide  
 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-  
 aminodibenzofuran-1-carboxamide 685874-99-1P,  
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxydibenzofuran-1-

carboxamide 685875-00-7P,  
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-cyanodibenzofuran-1-carboxamide  
 685875-05-2P, N-Benzyl-4-cyclopentyloxydibenzofuran-1-carboxamide  
 685875-06-3P, 4-[4-[(Cyclopentyl)oxy]dibenzofuran-1-  
 ylcarboxamido]pyridine 685875-08-5P,  
 4-(4-Methylsulfanyldibenzofuran-1-ylcarboxamido)pyridine  
 685875-09-6P, N-(4-Methoxydibenzofuran-1-yl)nicotinamide  
 685875-10-9P, N-Benzyl-4-methoxydibenzofuran-1-sulfonamide  
 685875-11-0P, 4-(((4-Methoxydibenzofuran-1-  
 yl)sulfonyl)amino)pyridine 685875-12-1P 685875-13-2P  
 685875-15-4P, 1-Methoxy-4-(((4-methoxyphenyl)amino)sulfonyl)-9H-  
 carbazole 685875-20-1P 685875-21-2P,  
 1-Methoxy-4-[(pyridin-4-yl)amino]sulfonyl]-9H-carbazole  
 685875-22-3P, N-(2,6-Dichlorophenyl)-1-methoxy-9H-4-  
 carbazolsulfonamide 685875-23-4P,  
 N-(2,6-Dichlorophenyl)-9-formyl-1-methoxy-9H-4-carbazolsulfonamide  
 685875-24-5P, N-(Pyridin-4-yl)-1-methoxy-9H-4-carbazolecarboxamide  
 685875-25-6P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-26-7P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-1-methoxy-9H-4-carbazolecarboxamide  
 685875-30-3P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-6-chloro-1-  
 methoxy-9H-4-carbazolecarboxamide 685875-32-5P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-34-7P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-36-9P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-methoxybenzyl)-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-38-1P,  
 N-(3,5-Dichloropyridin-4-yl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-41-6P,  
 N-(4-Pyridyl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide  
 685875-44-9P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-48-3P,  
 N-(3,5-Dichloropyridin-4-yl)-9-benzyl-1-ethoxy-9H-4-carbazolecarboxamide  
 685875-52-9P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-6-chloro-1-  
 ethoxy-9H-4-carbazolecarboxamide 685875-56-3P,  
 N-(4-Pyridyl)-9-benzyl-1-ethoxy-9H-4-carbazolecarboxamide  
 685875-57-4P, N-(3-Pyridyl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-  
 9H-4-carbazolecarboxamide 685875-58-5P,  
 N-(4-Pyridyl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-59-6P,  
 N-(3,5-Dichloropyridin-4-yl)-8-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-63-2P,  
 N-(3,5-Dichloropyridin-4-yl)-8-chloro-9-(4-Fluorobenzyl)-1-methoxy-9H-4-  
 carbazolecarboxamide 685875-67-6P,  
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-1-methoxy-9-methyl-9H-4-  
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 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-  
 9H-4-carbazolecarboxamide 685875-72-3P,  
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 9H-4-carbazolecarboxamide 685875-73-4P,  
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 9H-4-carbazolecarboxamide 685875-74-5P,  
 N-(3,5-Dichloropyridin-4-yl)-9-methyl-1-methoxy-9H-4-carbazolecarboxamide  
 685875-81-4P 685875-82-5P,  
 N-(4-Chlorophenyl)-4-methoxydibenzothiophene-1-carboxamide  
 685875-83-6P 685875-84-7P 685875-85-8P  
 685875-86-9P 685875-87-0P 685875-89-2P  
 685875-90-5P 685875-92-7P 685875-93-8P  
 685875-94-9P 685875-98-3P 685875-99-4P

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685876-00-0P 685876-01-1P 685876-02-2P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-(2-oxopyrrolidin-1-yl)dibenzofuran-1-carboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

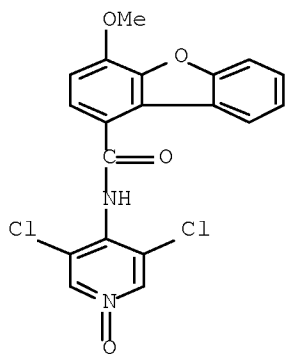
THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

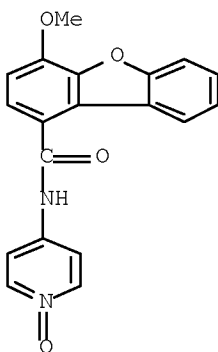
RN 685874-43-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-  
(CA INDEX NAME)



RN 685874-45-7 ZCAPLUS

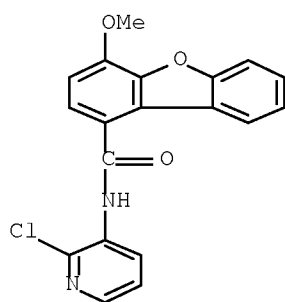
CN 1-Dibenzofurancarboxamide, 4-methoxy-N-(1-oxido-4-pyridinyl)- (CA INDEX NAME)



RN 685874-46-8 ZCAPLUS

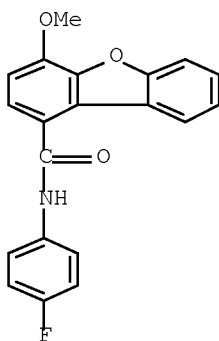
CN 1-Dibenzofurancarboxamide, N-(2-chloro-3-pyridinyl)-4-methoxy- (CA INDEX NAME)

10/524815



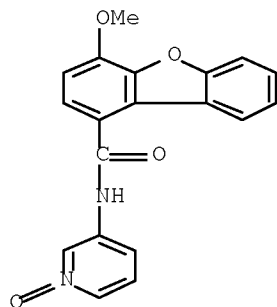
RN 685874-47-9 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(4-fluorophenyl)-4-methoxy- (CA INDEX NAME)



RN 685874-49-1 ZCAPLUS

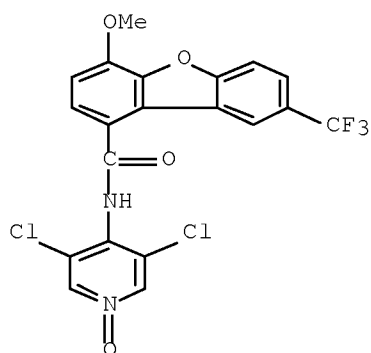
CN 1-Dibenzofurancarboxamide, 4-methoxy-N-(1-oxido-3-pyridinyl)- (CA INDEX NAME)



RN 685874-51-5 ZCAPLUS

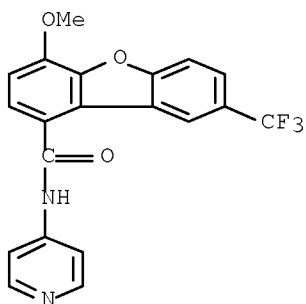
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-8-(trifluoromethyl)- (CA INDEX NAME)

10/524815



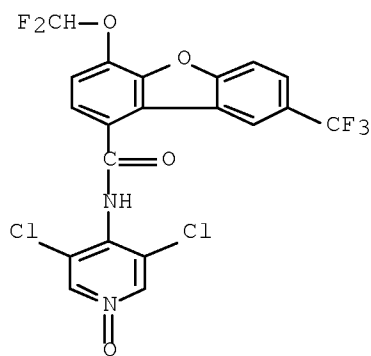
RN 685874-52-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-methoxy-N-4-pyridinyl-8-(trifluoromethyl)-  
(CA INDEX NAME)



RN 685874-54-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-  
(difluoromethoxy)-8-(trifluoromethyl)- (CA INDEX NAME)

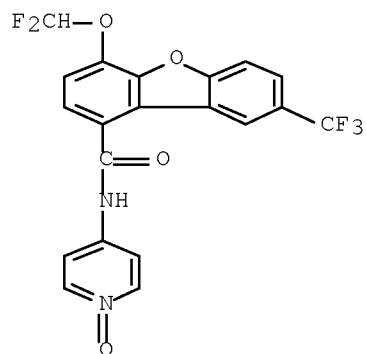


RN 685874-56-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-4-pyridinyl)-8-

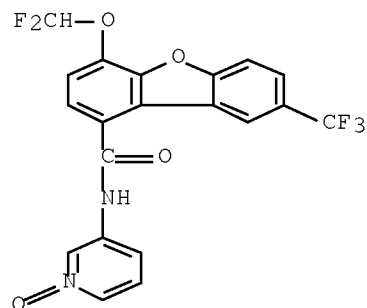
10/524815

(trifluoromethyl)- (CA INDEX NAME)



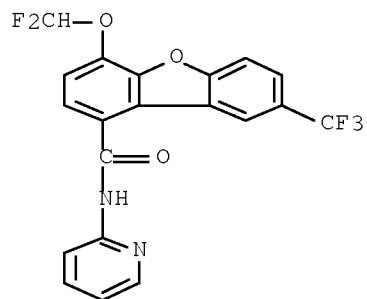
RN 685874-58-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-3-pyridinyl)-8-(trifluoromethyl)- (CA INDEX NAME)



RN 685874-59-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-2-pyridinyl-8-(trifluoromethyl)- (CA INDEX NAME)

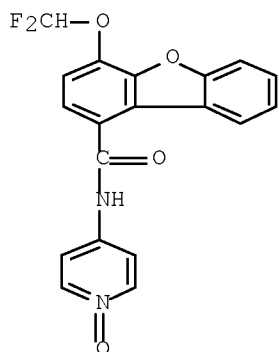


RN 685874-62-8 ZCAPLUS



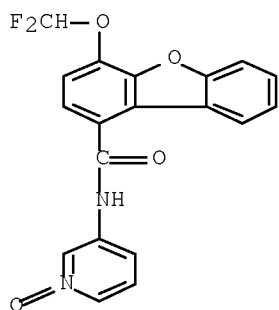
10/524815

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-4-pyridinyl)-  
(CA INDEX NAME)



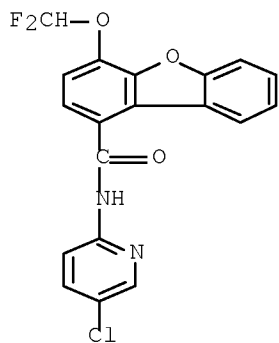
RN 685874-64-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-3-pyridinyl)-  
(CA INDEX NAME)



RN 685874-65-1 ZCAPLUS

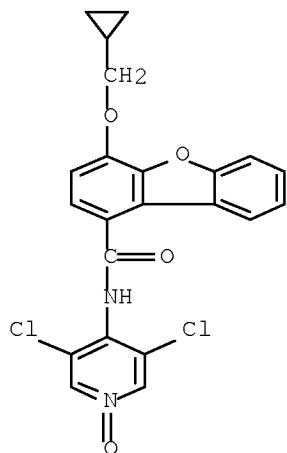
CN 1-Dibenzofurancarboxamide, N-(5-chloro-2-pyridinyl)-4-(difluoromethoxy)-  
(CA INDEX NAME)



10/524815

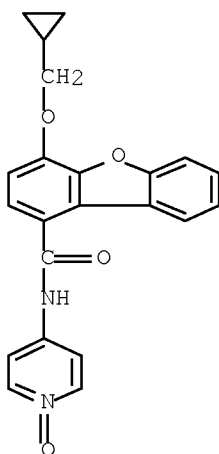
RN 685874-67-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(3,5-dichloro-1-oxido-4-pyridinyl)- (CA INDEX NAME)



RN 685874-69-5 ZCAPLUS

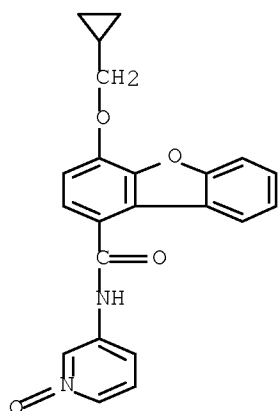
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(1-oxido-4-pyridinyl)- (CA INDEX NAME)



RN 685874-71-9 ZCAPLUS

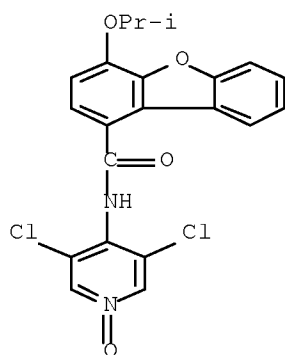
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(1-oxido-3-pyridinyl)- (CA INDEX NAME)

10/524815



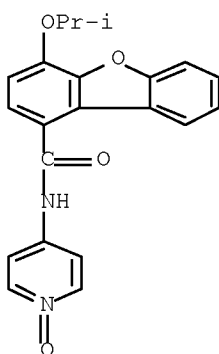
RN 685874-73-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-(1-methylethoxy)- (CA INDEX NAME)



RN 685874-75-3 ZCAPLUS

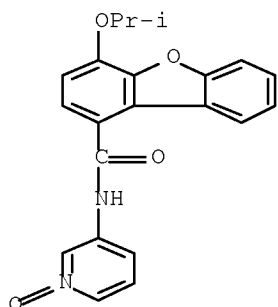
CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-(1-oxido-4-pyridinyl)- (CA INDEX NAME)



10/524815

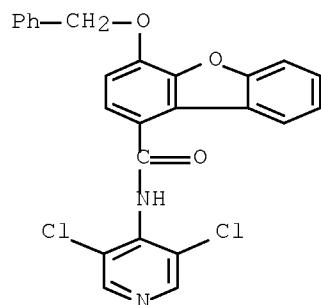
RN 685874-77-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-(1-oxido-3-pyridinyl)-  
(CA INDEX NAME)



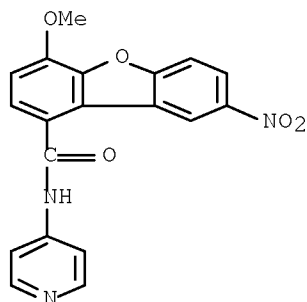
RN 685874-78-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(phenylmethoxy)-  
(CA INDEX NAME)



RN 685874-80-0 ZCAPLUS

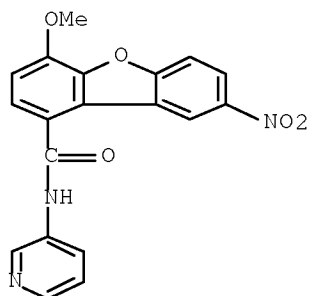
CN 1-Dibenzofurancarboxamide, 4-methoxy-8-nitro-N-4-pyridinyl- (CA INDEX  
NAME)



10/524815

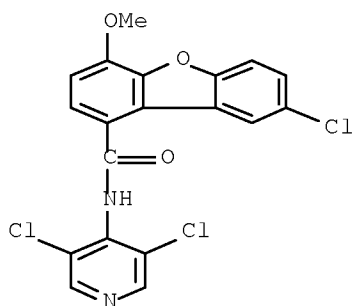
RN 685874-81-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-methoxy-8-nitro-N-3-pyridinyl- (CA INDEX NAME)



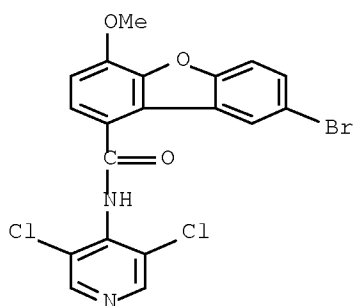
RN 685874-82-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-chloro-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 685874-83-3 ZCAPLUS

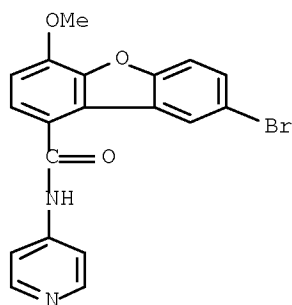
CN 1-Dibenzofurancarboxamide, 8-bromo-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



10/524815

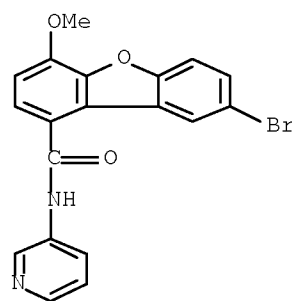
RN 685874-84-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-bromo-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



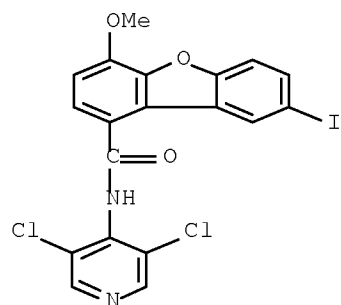
RN 685874-85-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-bromo-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 685874-86-6 ZCAPLUS

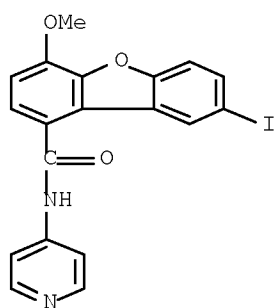
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-iodo-4-methoxy- (CA INDEX NAME)



10/524815

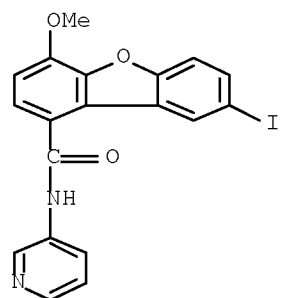
RN 685874-87-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-iodo-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



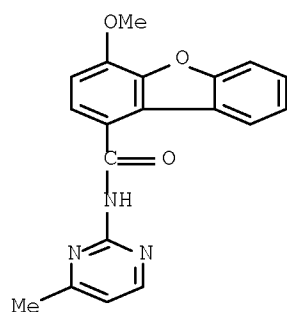
RN 685874-88-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-iodo-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 685874-89-9 ZCAPLUS

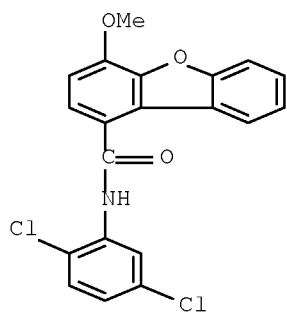
CN 1-Dibenzofurancarboxamide, 4-methoxy-N-(4-methyl-2-pyrimidinyl)- (CA INDEX NAME)



RN 685874-90-2 ZCAPLUS

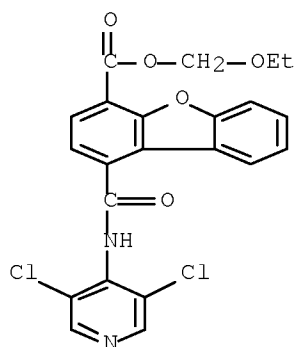
10/524815

CN 1-Dibenzofurancarboxamide, N-(2,5-dichlorophenyl)-4-methoxy- (CA INDEX NAME)



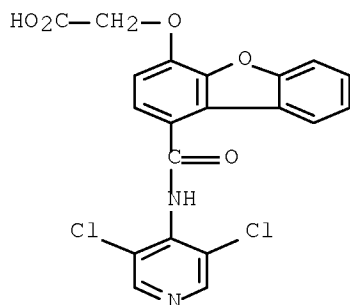
RN 685874-91-3 ZCAPLUS

CN 4-Dibenzofurancarboxylic acid, 1-[[ (3,5-dichloro-4-pyridinyl)amino]carbonyl]-, ethoxymethyl ester (CA INDEX NAME)



RN 685874-92-4 ZCAPLUS

CN Acetic acid, 2-[[1-[[ (3,5-dichloro-4-pyridinyl)amino]carbonyl]-4-dibenzofuranyl]oxy]- (CA INDEX NAME)

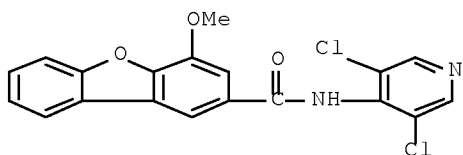


RN 685874-93-5 ZCAPLUS



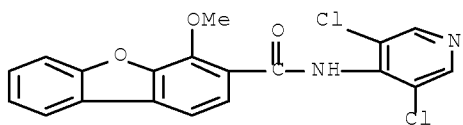
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CN 2-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA  
INDEX NAME)



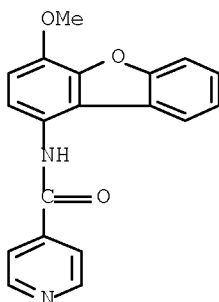
RN 685874-94-6 ZCAPLUS

CN 3-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA  
INDEX NAME)



RN 685874-95-7 ZCAPLUS

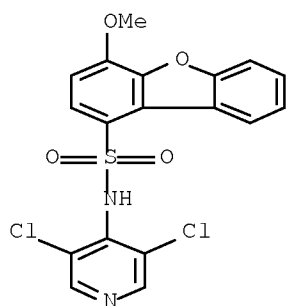
CN 4-Pyridinecarboxamide, N-(4-methoxy-1-dibenzofuranyl)- (CA INDEX NAME)



RN 685874-96-8 ZCAPLUS

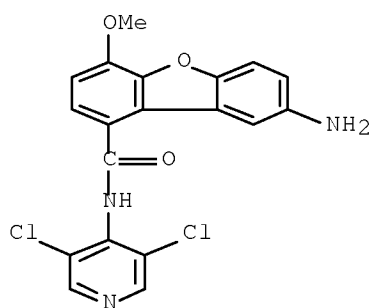
CN 1-Dibenzofuransulfonamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA  
INDEX NAME)

10/524815



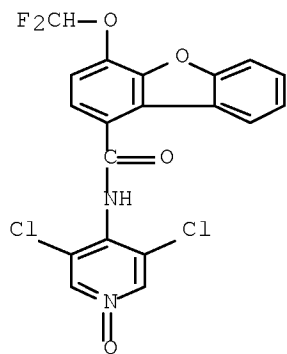
RN 685874-98-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-amino-N-(3,5-dichloro-4-pyridinyl)-4-methoxy-  
(CA INDEX NAME)



RN 685874-99-1 ZCAPLUS

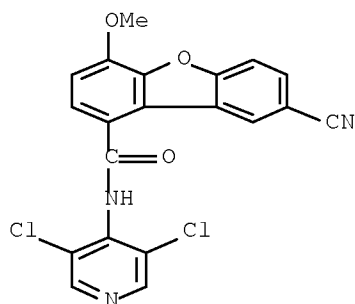
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-  
(difluoromethoxy)- (CA INDEX NAME)



RN 685875-00-7 ZCAPLUS

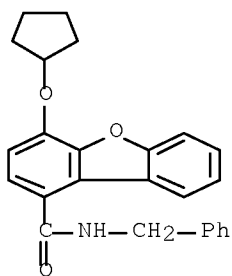
CN 1-Dibenzofurancarboxamide, 8-cyano-N-(3,5-dichloro-4-pyridinyl)-4-methoxy-  
(CA INDEX NAME)

10/524815



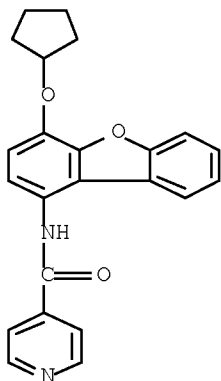
RN 685875-05-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopentyloxy)-N-(phenylmethyl)- (CA INDEX NAME)



RN 685875-06-3 ZCAPLUS

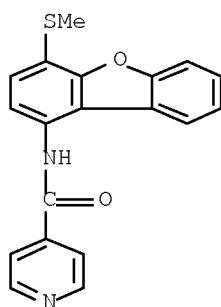
CN 4-Pyridinecarboxamide, N-[4-(cyclopentyloxy)-1-dibenzofuranyl]- (CA INDEX NAME)



RN 685875-08-5 ZCAPLUS

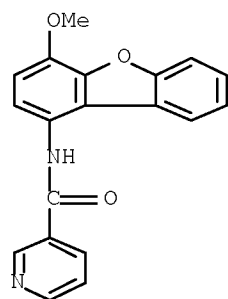
CN 4-Pyridinecarboxamide, N-[4-(methylthio)-1-dibenzofuranyl]- (CA INDEX NAME)

10/524815



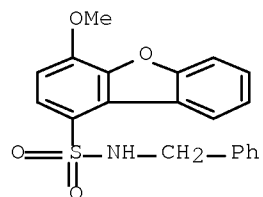
RN 685875-09-6 ZCAPLUS

CN 3-Pyridinecarboxamide, N-(4-methoxy-1-dibenzofuranyl)- (CA INDEX NAME)



RN 685875-10-9 ZCAPLUS

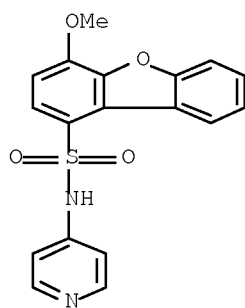
CN 1-Dibenzofuransulfonamide, 4-methoxy-N-(phenylmethyl)- (CA INDEX NAME)



RN 685875-11-0 ZCAPLUS

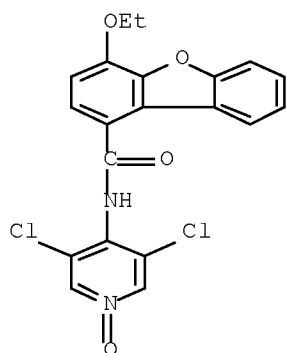
CN 1-Dibenzofuransulfonamide, 4-methoxy-N-4-pyridinyl- (CA INDEX NAME)

10/524815



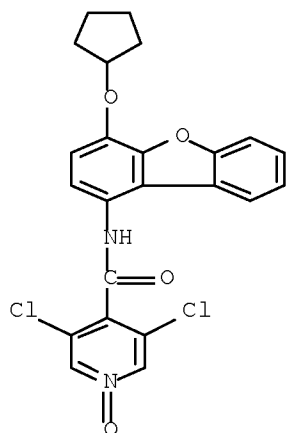
RN 685875-12-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-ethoxy-  
(CA INDEX NAME)



RN 685875-13-2 ZCAPLUS

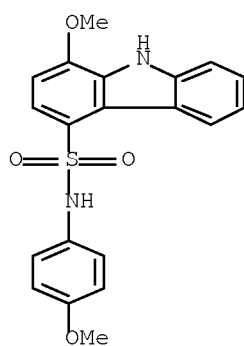
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-[4-(cyclopentyloxy)-1-dibenzofuranyl]-, 1-oxide (CA INDEX NAME)



10/524815

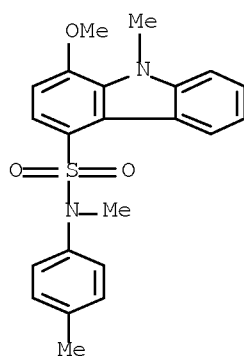
RN 685875-15-4 ZCAPLUS

CN 9H-Carbazole-4-sulfonamide, 1-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



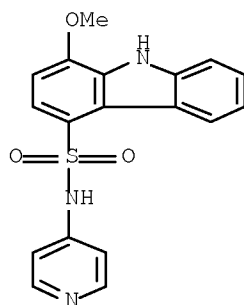
RN 685875-20-1 ZCAPLUS

CN 9H-Carbazole-4-sulfonamide, 1-methoxy-N,9-dimethyl-N-(4-methylphenyl)- (CA INDEX NAME)



RN 685875-21-2 ZCAPLUS

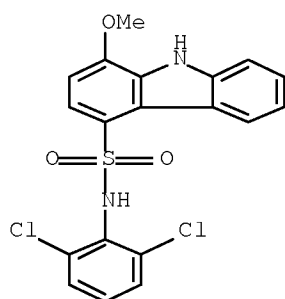
CN 9H-Carbazole-4-sulfonamide, 1-methoxy-N-4-pyridinyl- (CA INDEX NAME)



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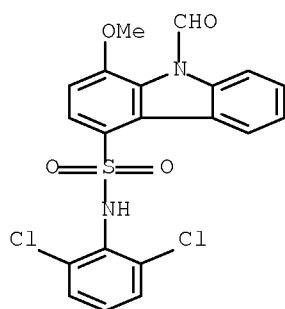
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CN 9H-Carbazole-4-sulfonamide, N-(2,6-dichlorophenyl)-1-methoxy- (CA INDEX NAME)



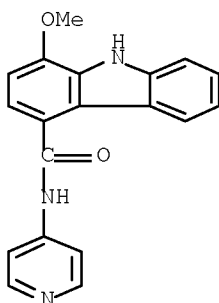
RN 685875-23-4 ZCAPLUS

CN 9H-Carbazole-4-sulfonamide, N-(2,6-dichlorophenyl)-9-formyl-1-methoxy- (CA INDEX NAME)



RN 685875-24-5 ZCAPLUS

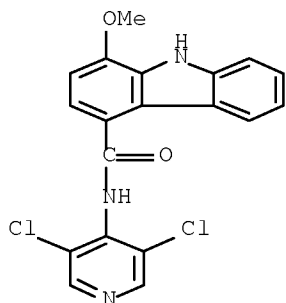
CN 9H-Carbazole-4-carboxamide, 1-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 685875-25-6 ZCAPLUS

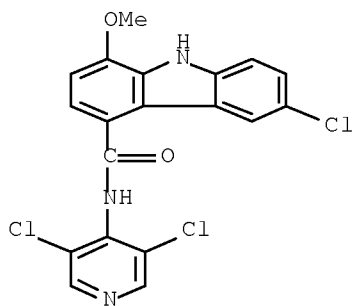
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CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy- (CA INDEX NAME)



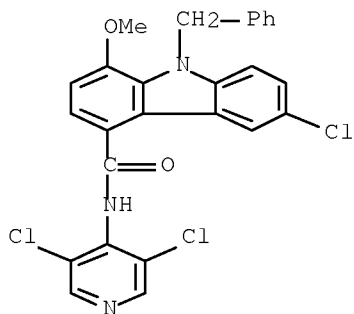
RN 685875-26-7 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-methoxy- (CA INDEX NAME)



RN 685875-30-3 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-(phenylmethyl)- (CA INDEX NAME)



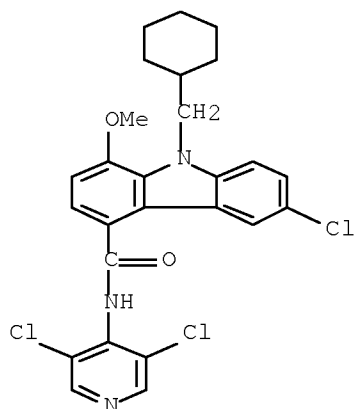
RN 685875-32-5 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-9-(cyclohexylmethyl)-N-(3,5-dichloro-



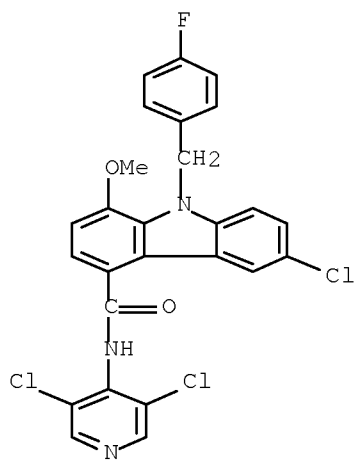
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4-pyridinyl)-1-methoxy- (CA INDEX NAME)



RN 685875-34-7 ZCAPLUS

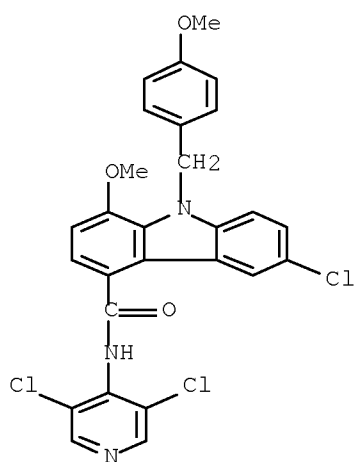
CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-9-[(4-fluorophenyl)methyl]-1-methoxy- (CA INDEX NAME)



RN 685875-36-9 ZCAPLUS

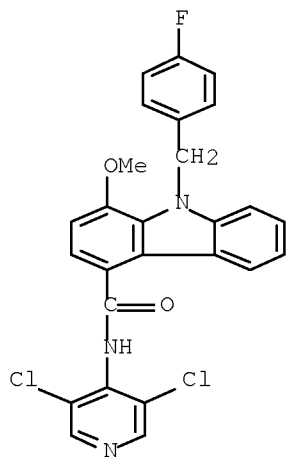
CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-[(4-methoxyphenyl)methyl]- (CA INDEX NAME)

10/524815



RN 685875-38-1 ZCAPLUS

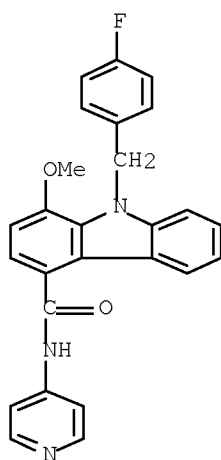
CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-9-[(4-fluorophenyl)methyl]-1-methoxy- (CA INDEX NAME)



RN 685875-41-6 ZCAPLUS

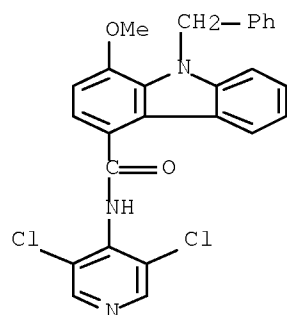
CN 9H-Carbazole-4-carboxamide, 9-[(4-fluorophenyl)methyl]-1-methoxy-N-4-pyridinyl- (CA INDEX NAME)

10/524815



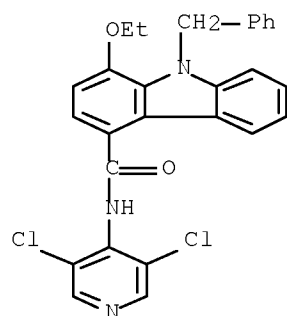
RN 685875-44-9 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-(phenylmethyl)- (CA INDEX NAME)



RN 685875-48-3 ZCAPLUS

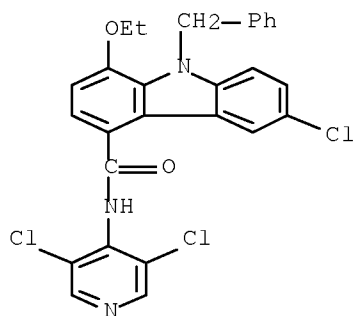
CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-ethoxy-9-(phenylmethyl)- (CA INDEX NAME)



RN 685875-52-9 ZCAPLUS

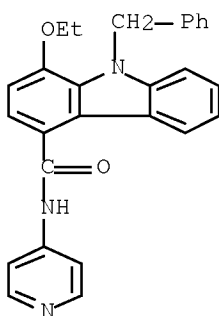
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CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-ethoxy-9-(phenylmethyl)- (CA INDEX NAME)



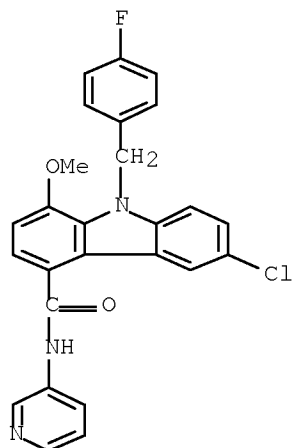
RN 685875-56-3 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 1-ethoxy-9-(phenylmethyl)-N-4-pyridinyl- (CA INDEX NAME)



RN 685875-57-4 ZCAPLUS

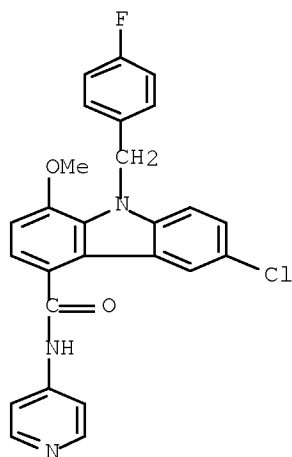
CN 9H-Carbazole-4-carboxamide, 6-chloro-9-[(4-fluorophenyl)methyl]-1-methoxy-N-3-pyridinyl- (CA INDEX NAME)



10/524815

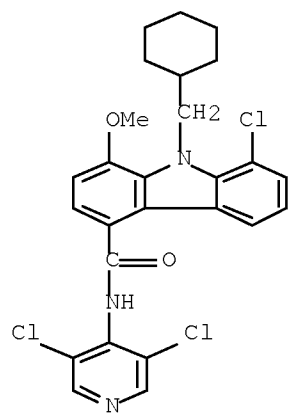
RN 685875-58-5 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-9-[(4-fluorophenyl)methyl]-1-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 685875-59-6 ZCAPLUS

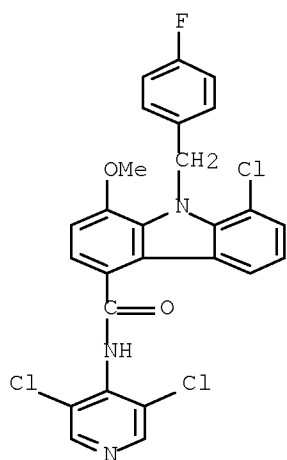
CN 9H-Carbazole-4-carboxamide, 8-chloro-9-(cyclohexylmethyl)-N-(3,5-dichloro-4-pyridinyl)-1-methoxy- (CA INDEX NAME)



RN 685875-63-2 ZCAPLUS

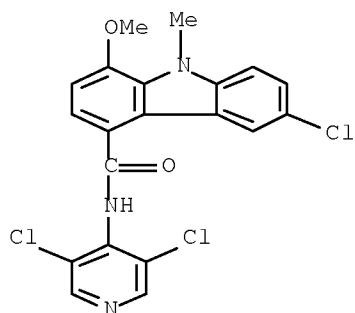
CN 9H-Carbazole-4-carboxamide, 8-chloro-N-(3,5-dichloro-4-pyridinyl)-9-[(4-fluorophenyl)methyl]-1-methoxy- (CA INDEX NAME)

10/524815



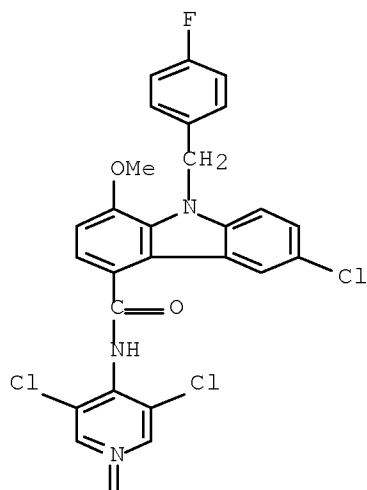
RN 685875-67-6 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl- (CA INDEX NAME)

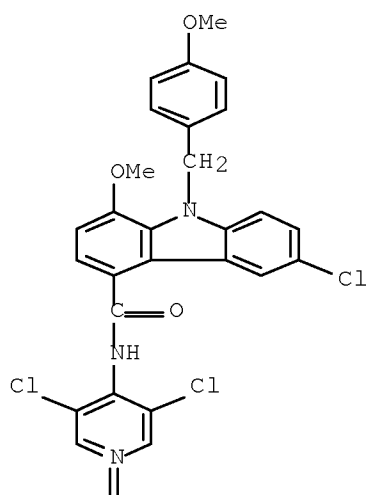


RN 685875-71-2 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-1-oxido-4-pyridinyl)-9-[(4-fluorophenyl)methyl]-1-methoxy- (CA INDEX NAME)



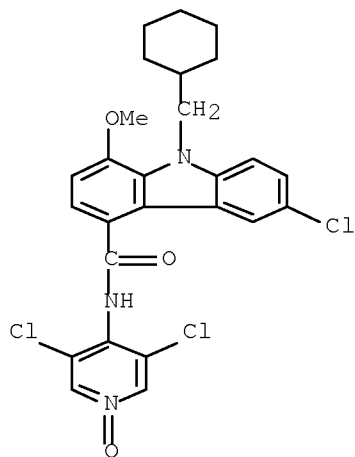
RN 685875-72-3 ZCAPLUS  
 CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-1-oxido-4-pyridinyl)-  
 1-methoxy-9-[(4-methoxyphenyl)methyl]- (CA INDEX NAME)





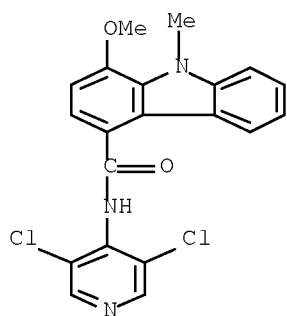
RN 685875-73-4 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-9-(cyclohexylmethyl)-N-(3,5-dichloro-1-oxido-4-pyridinyl)-1-methoxy- (CA INDEX NAME)



RN 685875-74-5 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl- (CA INDEX NAME)

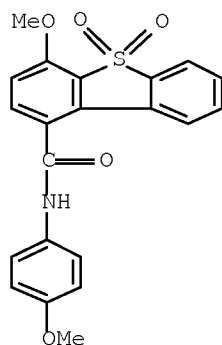


RN 685875-81-4 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, 4-methoxy-N-(4-methoxyphenyl)-, 5,5-dioxide (CA INDEX NAME)

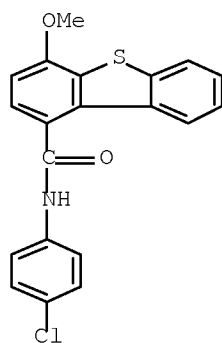


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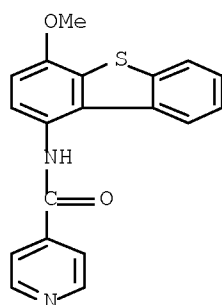
RN 685875-82-5 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, N-(4-chlorophenyl)-4-methoxy- (CA INDEX NAME)



RN 685875-83-6 ZCAPLUS

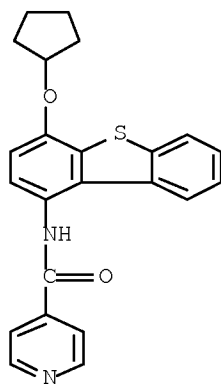
CN 4-Pyridinecarboxamide, N-(4-methoxy-1-dibenzothienyl)- (CA INDEX NAME)



RN 685875-84-7 ZCAPLUS

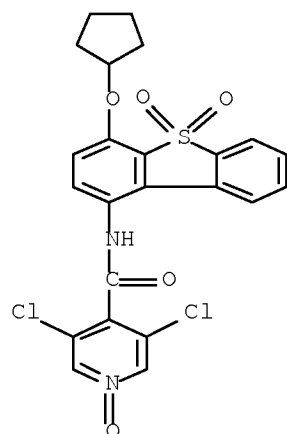
CN 4-Pyridinecarboxamide, N-[4-(cyclopentyloxy)-1-dibenzothienyl]- (CA INDEX NAME)

10/524815



RN 685875-85-8 ZCAPLUS

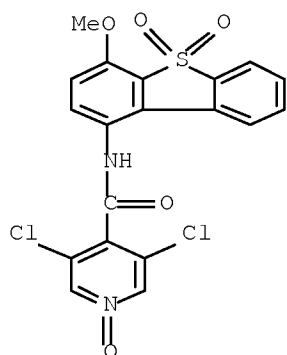
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-[4-(cyclopentyloxy)-5,5-dioxido-1-dibenzothienyl]-, 1-oxide (CA INDEX NAME)



RN 685875-86-9 ZCAPLUS

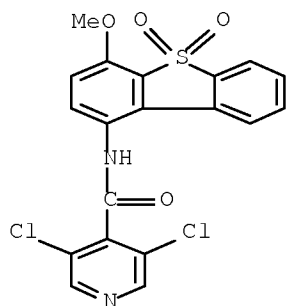
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-(4-methoxy-5,5-dioxido-1-dibenzothienyl)-, 1-oxide (CA INDEX NAME)

10/524815



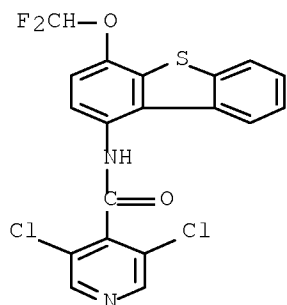
RN 685875-87-0 ZCAPLUS

CN 4-Pyridinecarboxamide, 3,5-dichloro-N-(4-methoxy-5,5-dioxido-1-dibenzothienyl)- (CA INDEX NAME)



RN 685875-89-2 ZCAPLUS

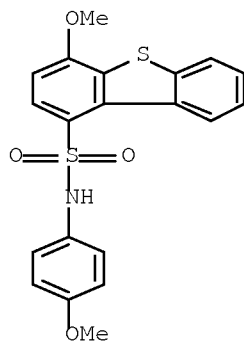
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-[4-(difluoromethoxy)-1-dibenzothienyl]- (CA INDEX NAME)



RN 685875-90-5 ZCAPLUS

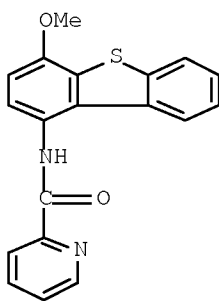
CN 1-Dibenzothiophenesulfonamide, 4-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)

10/524815



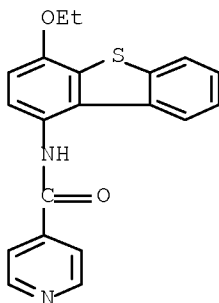
RN 685875-92-7 ZCAPLUS

CN 2-Pyridinecarboxamide, N-(4-methoxy-1-dibenzothienyl)- (CA INDEX NAME)



RN 685875-93-8 ZCAPLUS

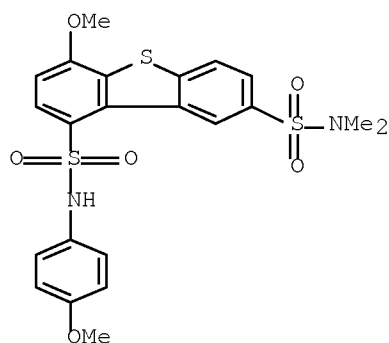
CN 4-Pyridinecarboxamide, N-(4-ethoxy-1-dibenzothienyl)- (CA INDEX NAME)



RN 685875-94-9 ZCAPLUS

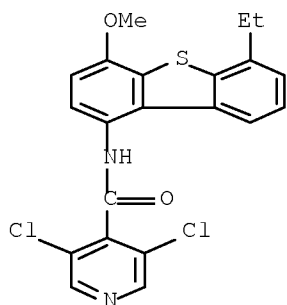
CN 1,8-Dibenzothiophenedisulfonamide, 4-methoxy-N1-(4-methoxyphenyl)-N8,N8-dimethyl- (CA INDEX NAME)

10/524815



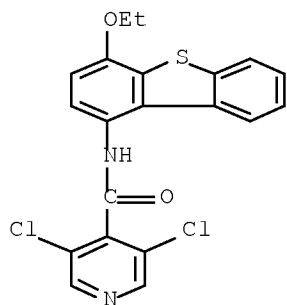
RN 685875-98-3 ZCAPLUS

CN 4-Pyridinecarboxamide, 3,5-dichloro-N-(6-ethyl-4-methoxy-1-dibenzothienyl)-  
(CA INDEX NAME)



RN 685875-99-4 ZCAPLUS

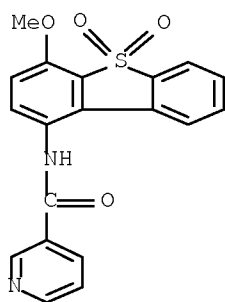
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-(4-ethoxy-1-dibenzothienyl)- (CA  
INDEX NAME)



RN 685876-00-0 ZCAPLUS

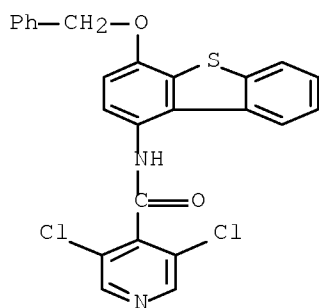
CN 3-Pyridinecarboxamide, N-(4-methoxy-5,5-dioxido-1-dibenzothienyl)- (CA  
INDEX NAME)

10/524815



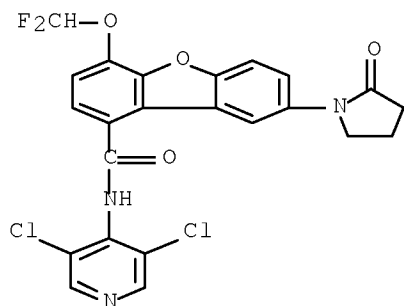
RN 685876-01-1 ZCAPLUS

CN 4-Pyridinecarboxamide, 3,5-dichloro-N-[4-(phenylmethoxy)-1-dibenzothienyl]-  
(CA INDEX NAME)



RN 685876-02-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-(2-oxo-1-pyrrolidinyl)- (CA INDEX NAME)



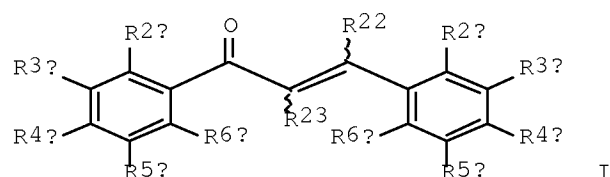
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RECORD (12 CITINGS)  
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 6 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN

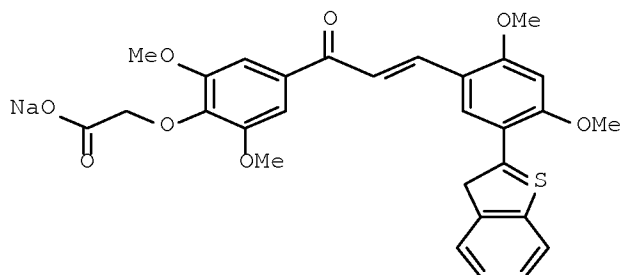
10/524815

ACCESSION NUMBER: 2001:935594 ZCAPLUS Full-text  
DOCUMENT NUMBER: 136:69730  
TITLE: Preparation of  
1,3-bis-(substituted-phenyl)-2-propen-1-ones as VCAM-1  
inhibitors for treatment of inflammatory disorders  
INVENTOR(S): Meng, Charles Q.; Ni, Liming; Sikorski, James A.;  
Hoong, Lee K.  
PATENT ASSIGNEE(S): Atherogenics, Inc., USA  
SOURCE: PCT Int. Appl., 220 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098291	A2	20011227	WO 2001-US19720	20010620 <--
WO 2001098291	A3	20020516		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2413878	A1	20011227	CA 2001-2413878	20010620 <--
BR 2001011889	A	20030624	BR 2001-11889	20010620 <--
EP 1330448	A2	20030730	EP 2001-946583	20010620 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 6608101	B1	20030819	US 2001-886348	20010620 <--
JP 2004501147	T	20040115	JP 2002-504247	20010620 <--
NZ 523443	A	20041126	NZ 2001-523443	20010620 <--
MX 2002012660	A	20040514	MX 2002-12660	20021218 <--
IN 2003DN00008	A	20060609	IN 2003-DN8	20030101 <--
ZA 2003000134	A	20051006	ZA 2003-134	20030106 <--
US 20030236298	A1	20031225	US 2003-443470	20030521 <--
US 7078431	B2	20060718		
ZA 2005003708	A	20070425	ZA 2005-3708	20050509 <--
US 20060258735	A1	20061116	US 2006-485940	20060713 <--
PRIORITY APPLN. INFO.:			US 2000-212769P	P 20000620 <--
			US 2000-255934P	P 20001215 <--
			US 2001-886348	A1 20010620 <--
			WO 2001-US19720	W 20010620 <--
			US 2003-443470	A1 20030521 <--
OTHER SOURCE(S):			MARPAT 136:69730	
GI				



I



II

AB Title compds. I [wherein R2a, R3a, R4a, R5a, R6a, R2b, R3b, R4b, R5b, and R6b = independently H, (cyclo)alkyl, (hetero)aryl, carbocyclyl, (halo)alkylthio, (un)substituted alkoxy or amino, (halo)acyl, amido, (halo)alkylsulfonyl, aminocarbonyl, alkenyl, alkynyl, halo, OH, SH, CN, NO<sub>2</sub>, SO<sub>3</sub>H, sulf(on)amido, PO<sub>3</sub>H<sub>2</sub>, alditol, carbohydrate, amino acid, etc.; R22 and R23 = independently H or alkyl; or R22 and R6a or R23 and R6a can join together to form a bridged carbocycle, (hetero)aryl, or heterocycle; R2a and R3a, R3a and R4a, R4a and R5a, R5a and R6a, R2b and R3b, R3b and R4b, R4b and R5b, or R5b and R6b and independently join to form a bridged (un)substituted carbocycle, cycloalkenyl, cycloalk(en)ylcarbonyl, (hetero)aryl, heterocycle, or alkylenedioxy; and the E or Z isomers thereof] were prepared to inhibit the expression of VCAM-1. For example, 3',5'-dimethoxy-4'-hydroxyacetophenone was treated with Et glycolate, PPh<sub>3</sub>, and di-Et azodicarboxylate in THF to give 4'-ethoxycarbonylmethoxy-3',5'-dimethoxyacetophenone (90%). Coupling the acetophenone and 5-(benzo[b]thien-2-yl)-2,4-dimethoxybenzaldehyde (preparation given) in the presence of NaOH in absolute EtOH afforded the 1,3-diphenyl-2-propen-1-one II (39%), which stimulated cultured human aortic smooth muscle cell activity with IC<sub>50</sub> of 0.45  $\mu$ M. I are useful for the treatment of inflammatory disorders that are mediated by VCAM-1, including arthritis, asthma, dermatitis, cystic fibrosis, post transplantation late and chronic solid organ rejection, multiple sclerosis, systemic lupus erythematosus, inflammatory bowel diseases, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, post-angioplasty restenosis, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves disease, gastrointestinal allergies, conjunctivitis, atherosclerosis, coronary artery disease, angina and small artery disease.

IC ICM C07D333-00

CC 27-8 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT Cystic fibrosis

Dermatitis

Graves' disease

Psoriasis

Transplant rejection

(treatment; preparation of bis(substituted phenyl)propenones as VCAM-1 inhibitors for treatment of inflammatory disorders)

IT Antidepressants

(tricyclic; co-administration of bis(substituted



phenyl)propenone VCAM-1 inhibitors with other biol. agents)

IT 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-88-2  
, Phenindamine 82-92-8, Marezine 86-22-6, Brompheniramine 91-84-9,  
Pyrilamine 113-92-8, Chlortrimeton 147-24-0, Benadryl 550-70-9,  
Actidil 969-33-5, Periactin 1229-35-2, Tacaryl  
2438-32-6, Polaramine 4330-99-8, Temaril 8064-07-1, Antivert  
14976-57-9, Tavist 50679-08-8, Seldane 68844-77-9, Hismanal  
79794-75-5, Claritin 153439-40-8, Allegra  
RL: PAC (Pharmacological activity); THU (Therapeutic  
use); BIOL (Biological study); USES (Uses)  
(co-administration of bis(substituted phenyl)propenone VCAM-1  
inhibitors with antihistamines)

IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone  
acetate 50-04-4, Cortisone Acetate 50-23-7,  
Hydrocortisone 50-24-8, Prednisolone 52-21-1,  
Prednisolone Acetate 52-39-1, Aldosterone 53-03-2,  
Prednisone 53-34-9, Fluprednisolone 53-36-1,  
Methylprednisolone Acetate 56-47-3, Deoxycortone Acetate  
67-73-2, Fluocinolone Acetonide 67-78-7, Triamcinolone  
Diacetate 76-25-5, Azmacort 79-61-8, Dichlorisone  
Acetate 83-43-2, Methylprednisolone 124-94-7,  
Triamcinolone 125-02-0, Prednisolone Sodium Phosphate  
125-03-1, Hydrocortamate Hydrochloride 125-04-2,  
Hydrocortisone Sodium Succinate 125-10-0, Prednisone Acetate  
151-73-5, Betamethasone Sodium Phosphate 152-97-6,  
Fluocortolone 303-40-2, Fluocortolone Hexanoate  
312-93-6, Dexamethasone Phosphate 356-12-7,  
Fluocinonide 378-44-9, Betamethasone 382-67-2,  
Desoxymethasone 426-13-1, Fluorometholone 508-99-6  
, Hydrocortisone Cypionate 514-36-3, Fludrocortisone Acetate  
599-33-7, Prednylidene 630-67-1 638-94-8,  
Desonide 808-48-0, Deoxycortone Pivalate 987-24-6,  
Betamethasone Acetate 1107-99-9, Prednisolone Pivalate  
1110-40-3, Cortivazol 1177-87-3, Dexamethasone Acetate  
1247-42-3, Meprednisone 1255-35-2, Fluprednidene  
Acetate 1524-88-5, Flurandrenolone 1597-82-6,  
Paramethasone Acetate 1715-33-9, Prednisolone Sodium Succinate  
2002-29-1, Flumethasone Pivalate 2135-17-3,  
Flumethasone 2152-44-5, Betamethasone Valerate  
2203-97-6, Hydrocortisone Hemisuccinate 2265-64-7,  
Dexamethasone Isonicotinate 2375-03-3, Methylprednisolone  
Sodium Succinate 2392-39-4, Dexamethasone Sodium Phosphate  
2668-66-8, Medrysone 2825-60-7, Formocortal  
2920-86-7, Prednisolone Hemisuccinate 2921-57-5,  
Methylprednisolone Hemisuccinate 3093-35-4, Halcinonide  
3385-03-3, Flunisolide 3693-39-8, Fluclorolone  
Acetonide 3801-06-7, Fluorometholone Acetate  
3936-02-5 5060-55-9, Prednisolone steaglate  
5251-34-3, Cloprednol 5534-09-8, Vanceril  
5593-20-4, Betamethasone Dipropionate 5611-51-8,  
Triamcinolone Hexacetonide 6000-74-4, Hydrocortisone Sodium  
Phosphate 7681-14-3, Prednisolone Tebutate  
13609-67-1, Hydrocortisone Butyrate 14484-47-0,  
Deflazacort 19888-56-3, Fluazacort 20423-99-8,  
Deprodone 22298-29-9, Betamethasone Benzoate  
23674-86-4, Difluprednate 25122-46-7, Clobetasol  
Propionate 25122-57-0, Clobetasone Butyrate  
29205-06-9, Fluocortolone Pivalate 33564-31-7,  
Diflorasone Diacetate 34097-16-0, Clocortolone Pivalate  
35100-44-8, Endrysone 41767-29-7, Fluocortin Butyl

10/524815

49697-38-3, Rimexolone 50629-82-8, Halometasone  
51022-69-6, Amcinonide 51333-22-3, Pulmicort  
53716-43-1, Bendacort 55560-96-8, Tixocortol Pivalate  
57524-89-7, Hydrocortisone Valerate 58497-00-0,  
Procinonide 58524-83-7, Ciprocinonide 59198-70-8,  
Diflucortolone Valerate 66734-13-2, Alclometasone Dipropionate  
66852-54-8, Halobetasol Propionate 66877-67-6,  
Domoprednate 69164-69-8 73771-04-7, Prednicarbate  
77326-96-6, Aerobid M 80474-14-2, Flovent  
83919-23-7, Mometasone Furoate 86022-88-0,  
Cyclomethasone

RL: PAC (Pharmacological activity); THU (Therapeutic  
use); BIOL (Biological study); USES (Uses)

(co-administration of bis(substituted phenyl)propenone VCAM-1  
inhibitors with corticosteroids)

IT 51-55-8, Atropine, biological studies 54-31-9, Frusemide 58-55-9,  
Theophylline, biological studies 59-05-2, Methotrexate 69-89-6D,  
Xanthine, derivs. 317-34-0, Aminophylline 2751-09-9, Troleandomycin  
4499-40-5, Cholel, biological studies 9003-98-9, DNAase 9005-49-6,  
Heparin, biological studies 12244-57-4, Myochrysine 15826-37-6, Sodium  
cromoglycate 21829-25-4, Nifedipine 22254-24-6, Atrovent  
30286-75-0, Oxitropium bromide 34580-13-7, Ketotifen  
59865-13-3, Cyclosporin 66357-35-5, Ranitidine 69049-74-7,  
Tilade 94470-67-4, Cromakalim 101975-10-4, Zardaverine  
104987-11-3, FK-506 107753-78-6, Accolate 111406-87-2,  
Zileuton

RL: PAC (Pharmacological activity); THU (Therapeutic  
use); BIOL (Biological study); USES (Uses)

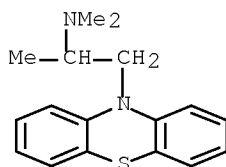
(co-administration of bis(substituted phenyl)propenone VCAM-1  
inhibitors with other biol. agents)

IT 60-87-7, Promethazine 82-88-2, Phenindamine  
969-33-5, Periactin 1229-35-2, Tacaryl  
4330-99-8, Temaril 79794-75-5, Claritin  
RL: PAC (Pharmacological activity); THU (Therapeutic  
use); BIOL (Biological study); USES (Uses)

(co-administration of bis(substituted phenyl)propenone VCAM-1  
inhibitors with antihistamines)

RN 60-87-7 ZCAPLUS

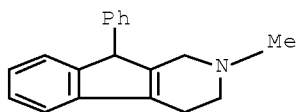
CN 10H-Phenothiazine-10-ethanamine, N,N, $\alpha$ -trimethyl- (CA INDEX NAME)



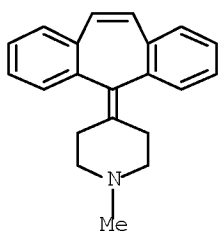
RN 82-88-2 ZCAPLUS

CN 1H-Indeno[2,1-c]pyridine, 2,3,4,9-tetrahydro-2-methyl-9-phenyl- (CA INDEX  
NAME)

10/524815

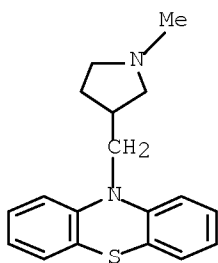


RN 969-33-5 ZCAPLUS  
CN Piperidine, 4-(5H-dibenzo[a,d]cyclohepten-5-ylidene)-1-methyl-,  
hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 1229-35-2 ZCAPLUS  
CN 10H-Phenothiazine, 10-[(1-methyl-3-pyrrolidinyl)methyl]-, hydrochloride  
(1:1) (CA INDEX NAME)



● HCl

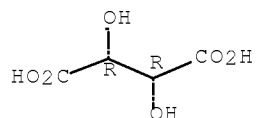
RN 4330-99-8 ZCAPLUS  
CN 10H-Phenothiazine-10-propanamine, N,N,β-trimethyl-,  
(2R,3R)-2,3-dihydroxybutanedioate (2:1) (CA INDEX NAME)

CM 1

CRN 87-69-4  
CMF C4 H6 O6

Absolute stereochemistry.

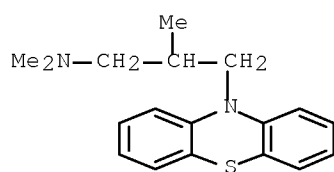
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CM 2

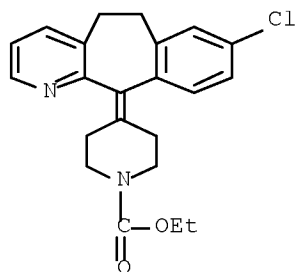
CRN 84-96-8

CMF C18 H22 N2 S



RN 79794-75-5 ZCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (CA INDEX NAME)



IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone  
acetate 50-04-4, Cortisone Acetate 50-23-7,  
Hydrocortisone 50-24-8, Prednisolone 52-21-1,  
Prednisolone Acetate 52-39-1, Aldosterone 53-03-2,  
Prednisone 53-34-9, Fluprednisolone 53-36-1,  
Methylprednisolone Acetate 56-47-3, Deoxycortone Acetate  
67-73-2, Fluocinolone Acetonide 67-78-7, Triamcinolone  
Diacetate 76-25-5, Azmacort 79-61-8, Dichlorisone  
Acetate 83-43-2, Methylprednisolone 124-94-7,  
Triamcinolone 125-02-0, Prednisolone Sodium Phosphate  
125-03-1, Hydrocortamate Hydrochloride 125-04-2,  
Hydrocortisone Sodium Succinate 125-10-0, Prednisone Acetate  
151-73-5, Betamethasone Sodium Phosphate 152-97-6,  
Fluocortolone 303-40-2, Fluocortolone Hexanoate

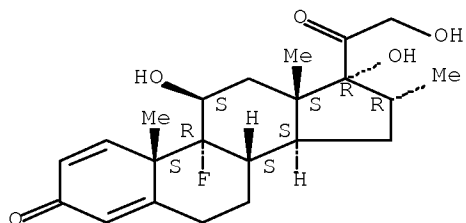
312-93-6, Dexamethasone Phosphate 356-12-7,  
 Fluocinonide 378-44-9, Betamethasone 382-67-2,  
 Desoxymethasone 426-13-1, Fluorometholone 508-99-6  
 , Hydrocortisone Cypionate 514-36-3, Fludrocortisone Acetate  
 599-33-7, Prednylidene 630-67-1 638-94-8,  
 Desonide 808-48-0, Deoxycortone Pivalate 987-24-6,  
 Betamethasone Acetate 1107-99-9, Prednisolone Pivalate  
 1110-40-3, Cortivazol 1177-87-3, Dexamethasone Acetate  
 1247-42-3, Meprednisone 1255-35-2, Fluprednidene  
 Acetate 1524-88-5, Flurandrenolone 1597-82-6,  
 Paramethasone Acetate 1715-33-9, Prednisolone Sodium Succinate  
 2002-29-1, Flumethasone Pivalate 2135-17-3,  
 Flumethasone 2152-44-5, Betamethasone Valerate  
 2203-97-6, Hydrocortisone Hemisuccinate 2265-64-7,  
 Dexamethasone Isonicotinate 2375-03-3, Methylprednisolone  
 Sodium Succinate 2392-39-4, Dexamethasone Sodium Phosphate  
 2668-66-8, Medrysone 2825-60-7, Formocortal  
 2920-86-7, Prednisolone Hemisuccinate 2921-57-5,  
 Methylprednisolone Hemisuccinate 3093-35-4, Halcinonide  
 3385-03-3, Flunisolide 3693-39-8, Fluclorolone  
 Acetonide 3801-06-7, Fluorometholone Acetate  
 3936-02-5 5060-55-9, Prednisolone steaglate  
 5251-34-3, Cloprednol 5534-09-8, Vanceril  
 5593-20-4, Betamethasone Dipropionate 5611-51-8,  
 Triamcinolone Hexacetonide 6000-74-4, Hydrocortisone Sodium  
 Phosphate 7681-14-3, Prednisolone Tebutate  
 13609-67-1, Hydrocortisone Butyrate 14484-47-0,  
 Deflazacort 19888-56-3, Fluazacort 20423-99-8,  
 Deprodone 22298-29-9, Betamethasone Benzoate  
 23674-86-4, Difluprednate 25122-46-7, Clobetasol  
 Propionate 25122-57-0, Clobetasone Butyrate  
 29205-06-9, Fluocortolone Pivalate 33564-31-7,  
 Diflorasone Diacetate 34097-16-0, Clolocortolone Pivalate  
 35100-44-8, Endrysone 41767-29-7, Fluocortin Butyl  
 49697-38-3, Rimexolone 50629-82-8, Halometasone  
 51022-69-6, Amcinonide 51333-22-3, Pulmicort  
 53716-43-1, Bendacort 55560-96-8, Tixocortol Pivalate  
 57524-89-7, Hydrocortisone Valerate 58497-00-0,  
 Procinnonide 58524-83-7, Ciprocinonide 59198-70-8,  
 Diflucortolone Valerate 66734-13-2, Alclometasone Dipropionate  
 66852-54-8, Halobetasol Propionate 66877-67-6,  
 Domoprednate 69164-69-8 73771-04-7, Prednicarbate  
 77326-96-6, Aerobid M 80474-14-2, Flovent  
 83919-23-7, Mometasone Furoate 86022-88-0,  
 Cyclomethasone  
 RL: PAC (Pharmacological activity); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (co-administration of bis(substituted phenyl)propenone VCAM-1  
 inhibitors with corticosteroids)

RN 50-02-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-,  
 (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

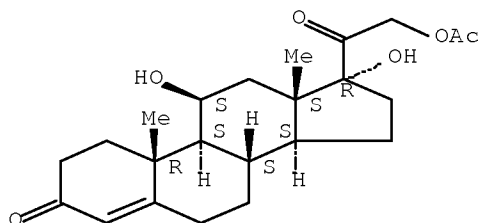
10/524815



RN 50-03-3 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-, (11β)- (CA INDEX NAME)

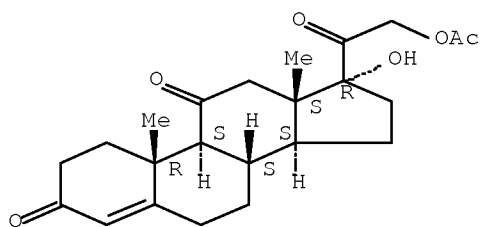
Absolute stereochemistry.



RN 50-04-4 ZCAPLUS

CN Pregn-4-ene-3,11,20-trione, 21-(acetyloxy)-17-hydroxy-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.

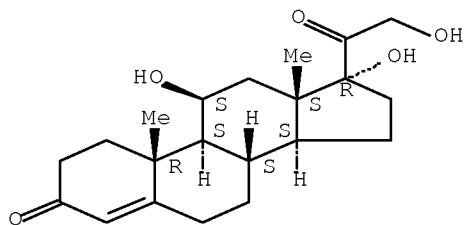


RN 50-23-7 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11β)- (CA INDEX NAME)

Absolute stereochemistry.

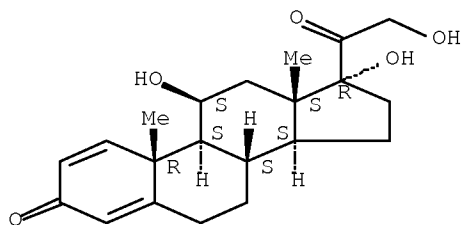
10/524815



RN 50-24-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-, (11β)- (CA INDEX NAME)

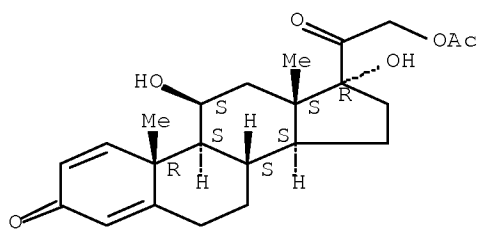
Absolute stereochemistry.



RN 52-21-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-, (11β)- (CA INDEX NAME)

Absolute stereochemistry.

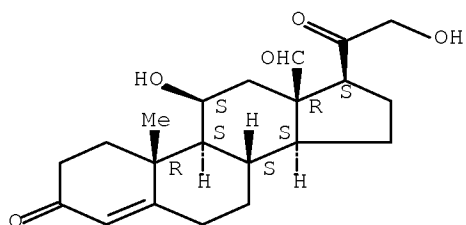


RN 52-39-1 ZCAPLUS

CN Pregn-4-en-18-al, 11,21-dihydroxy-3,20-dioxo-, (11β)- (CA INDEX NAME)

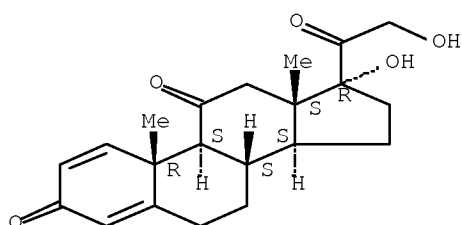
Absolute stereochemistry.

10/524815



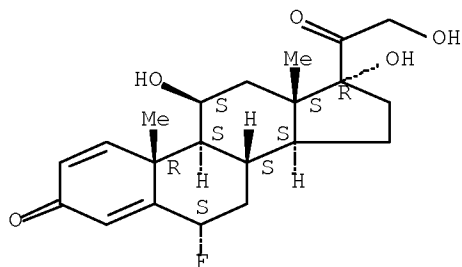
RN 53-03-2 ZCAPLUS  
CN Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy- (CA INDEX NAME)

Absolute stereochemistry.



RN 53-34-9 ZCAPLUS  
CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11,17,21-trihydroxy-,  
(6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

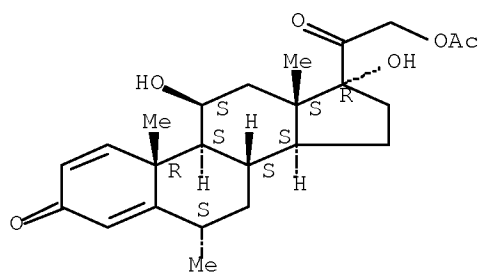


RN 53-36-1 ZCAPLUS  
CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-6-methyl-,  
(6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



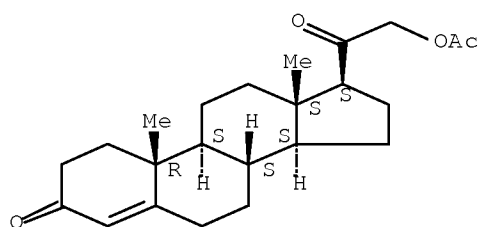
10/524815



RN 56-47-3 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(acetyloxy)- (CA INDEX NAME)

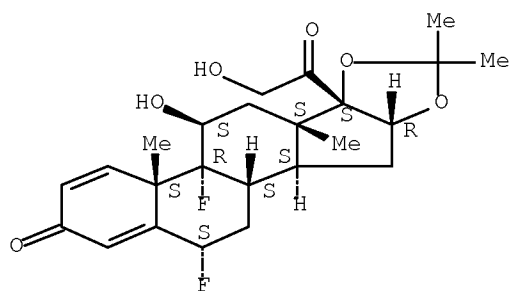
Absolute stereochemistry.



RN 67-73-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

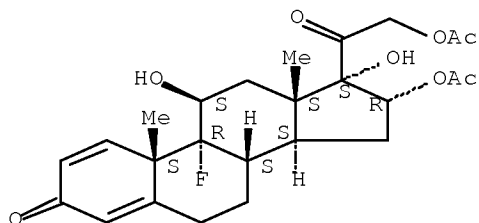


RN 67-78-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 16,21-bis(acetyloxy)-9-fluoro-11,17-dihydroxy-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

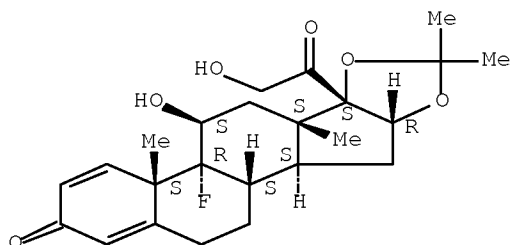
10/524815



RN 76-25-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

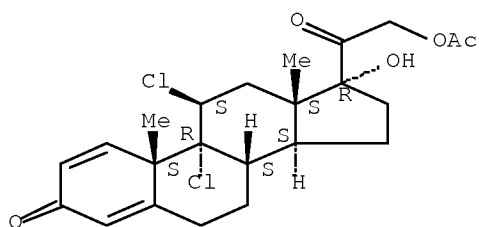
Absolute stereochemistry.



RN 79-61-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9,11-dichloro-17-hydroxy-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

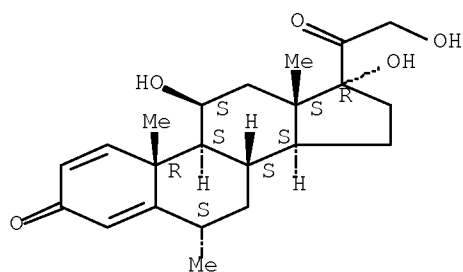


RN 83-43-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-6-methyl-, (6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

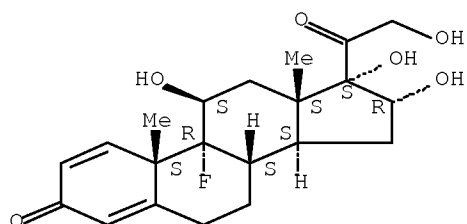
10/524815



RN 124-94-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,16,17,21-tetrahydroxy-,  
(11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

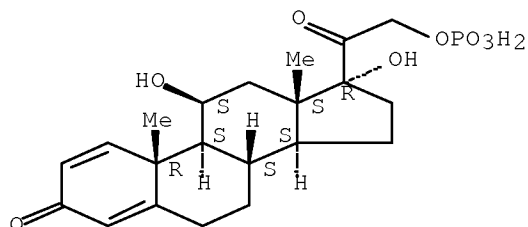
Absolute stereochemistry.



RN 125-02-0 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-(phosphonoxy)-, disodium  
salt, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



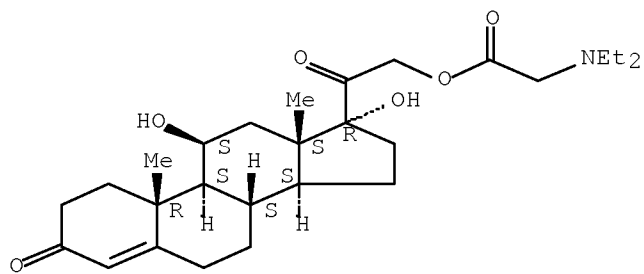
●2 Na

RN 125-03-1 ZCAPLUS

CN Glycine, N,N-diethyl-, (11 $\beta$ )-11,17-dihydroxy-3,20-dioxopregn-4-en-21-  
yl ester, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/524815

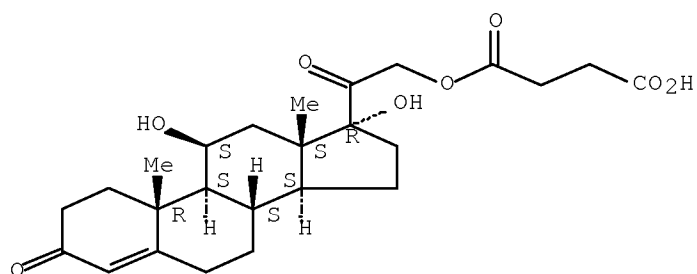


● HCl

RN 125-04-2 ZCAPLUS

CN Pregna-4-ene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, sodium salt (1:1), (11β)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

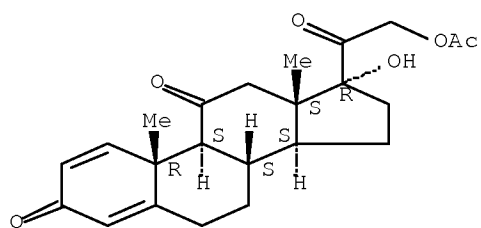


● Na

RN 125-10-0 ZCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 21-(acetyloxy)-17-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.



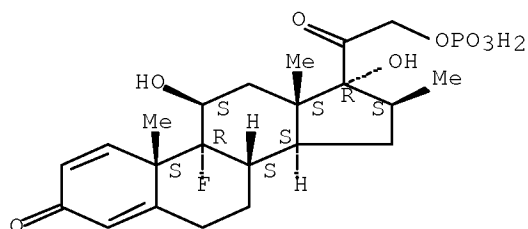
RN 151-73-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-

10/524815

(phosphonoxy)-, sodium salt (1:2), (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

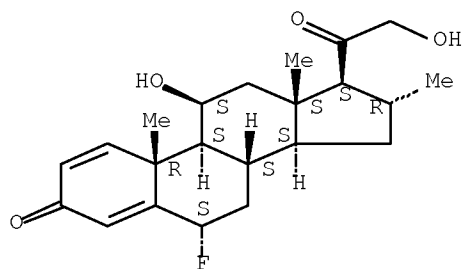


●2 Na

RN 152-97-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11,21-dihydroxy-16-methyl-,  
(6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

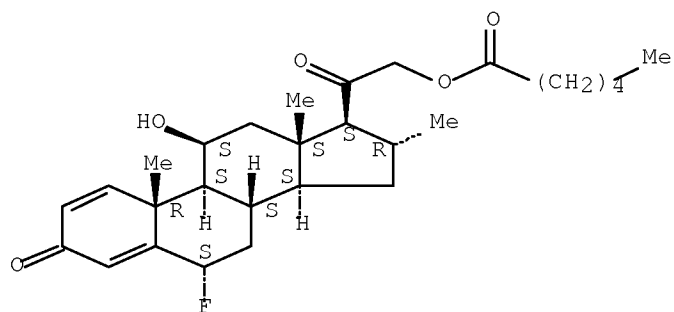
Absolute stereochemistry.



RN 303-40-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11-hydroxy-16-methyl-21-[(1-oxohexyl)oxy]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

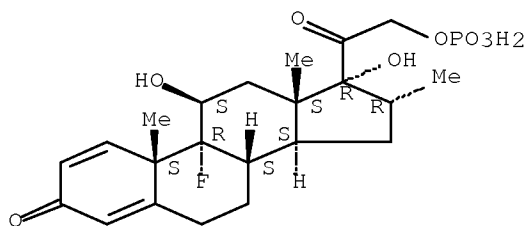


RN 312-93-6 ZCAPLUS

10/524815

CN    Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-(phosphonoxy)-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

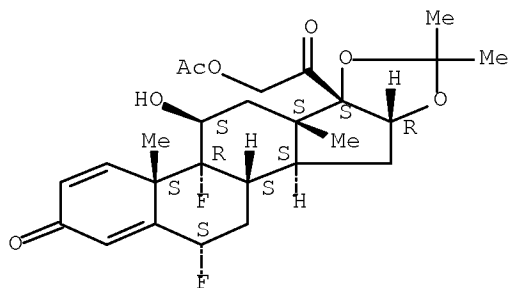
Absolute stereochemistry.



RN    356-12-7    ZCAPLUS

CN    Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

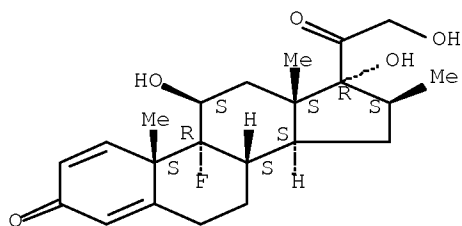
Absolute stereochemistry.



RN    378-44-9    ZCAPLUS

CN    Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



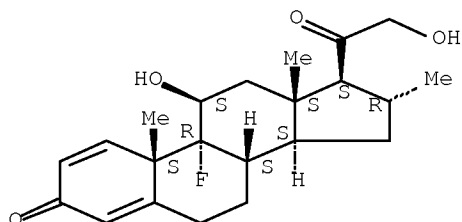
RN    382-67-2    ZCAPLUS

CN    Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16-methyl-,

10/524815

(11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

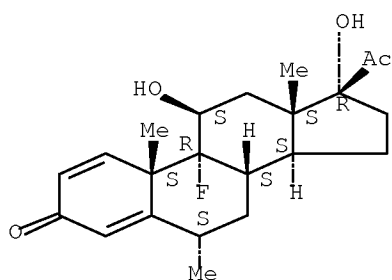
Absolute stereochemistry.



RN 426-13-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-6-methyl-,  
(6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

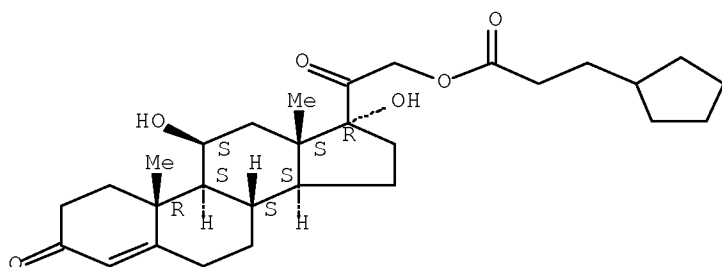
Absolute stereochemistry.



RN 508-99-6 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(3-cyclopentyl-1-oxopropoxy)-11,17-dihydroxy-,  
(11 $\beta$ )- (CA INDEX NAME)

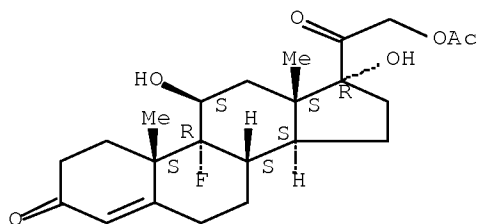
Absolute stereochemistry.



RN 514-36-3 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-,  
(11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



CN      Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-16-methylene-,  
 (11 $\beta$ )- (CA INDEX NAME)

The diagram shows a steroid nucleus with four fused rings (A, B, C, D). The A ring has a ketone group at C3 and a double bond between C4 and C5. The B ring has a methyl group at C10 (wedge) and a hydrogen at C13 (wedge). The C ring has a methyl group at C14 (wedge) and a hydrogen at C17 (wedge). The D ring has a methyl group at C18 (wedge) and a hydrogen at C19 (wedge). A complex side chain is attached at C17, consisting of a six-membered ring with a ketone group at C20, a double bond between C21 and C22, and a methyl group at C23 (wedge). The side chain also features a hydroxyl group at C24 (wedge) and a terminal vinyl group (CH2) at C25.

CN    Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(3-sulFOBenzoyl)oxy]-,  
sodium salt (1:1), (11 $\beta$ )- (CA INDEX NAME)

The chemical structure shows a steroid nucleus with a 3-sulfobenzoate ester group. The steroid core has a ketone at C-3, a methyl group at C-10 (Me), and a hydroxyl group at C-14 (HO). The ester group is attached to the C-17 position via a 2-hydroxyethyl linker. The benzoate ring has a sulfonate group (SO<sub>3</sub>H) at the 3-position. Stereochemistry is indicated with wedges and dashes at C-10, C-13, C-14, and C-17.

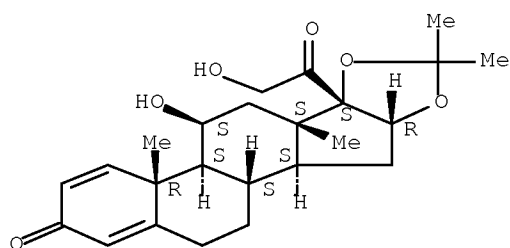


CN	Pregna-1,4-diene-3,20-dione, 11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)
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10/524815

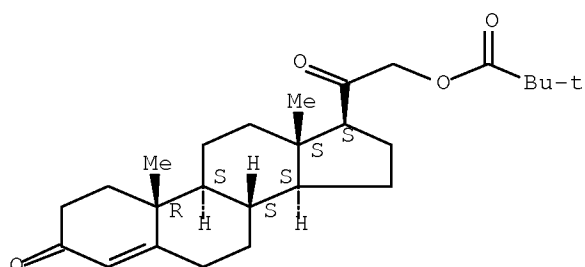
Absolute stereochemistry.



RN 808-48-0 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)- (CA INDEX NAME)

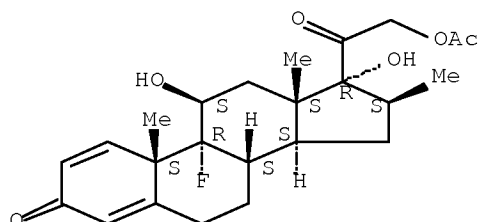
Absolute stereochemistry.



RN 987-24-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-methyl-, (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

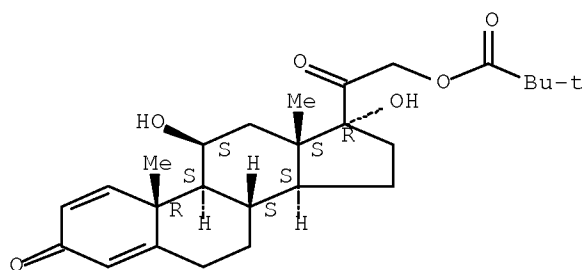


RN 1107-99-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)-11,17-dihydroxy-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

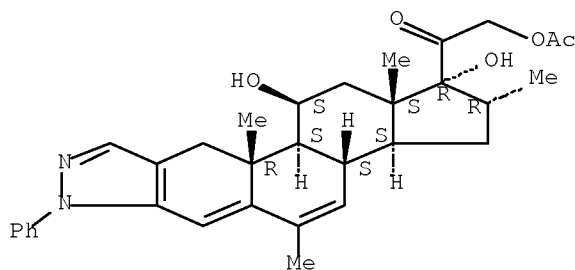
10/524815



RN 1110-40-3 ZCAPLUS

CN 2'-H-Pregna-2,4,6-trieno[3,2-c]pyrazol-20-one,  
21-(acetyloxy)-11,17-dihydroxy-6,16-dimethyl-2'-phenyl-,  
(11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

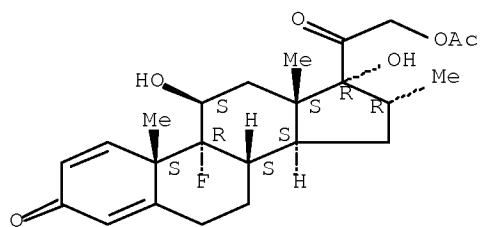
Absolute stereochemistry.



RN 1177-87-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-  
methyl-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

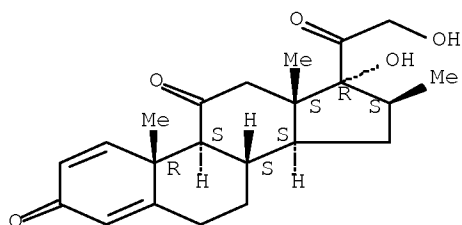


RN 1247-42-3 ZCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy-16-methyl-, (16 $\beta$ )-  
(CA INDEX NAME)

Absolute stereochemistry.

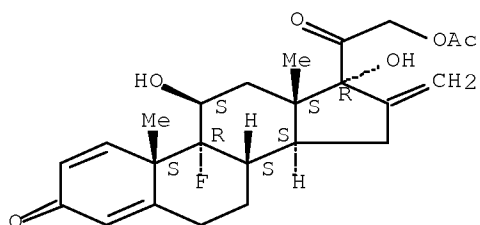
10/524815



RN 1255-35-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-methylene-, (11 $\beta$ )- (CA INDEX NAME)

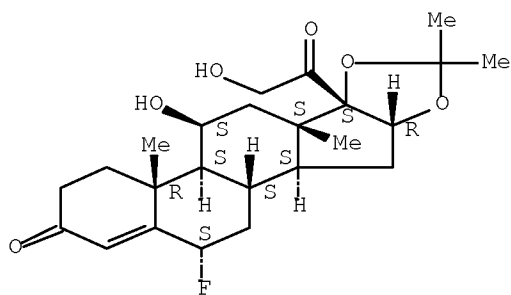
Absolute stereochemistry.



RN 1524-88-5 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

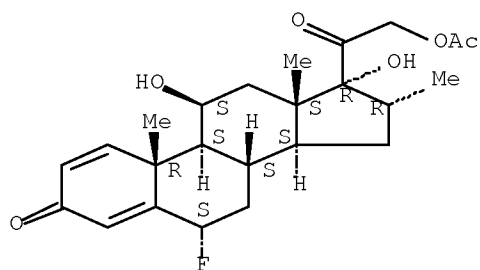


RN 1597-82-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-6-fluoro-11,17-dihydroxy-16-methyl-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

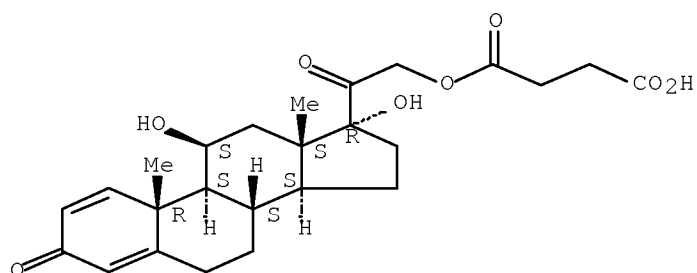
10/524815



RN 1715-33-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, monosodium salt, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

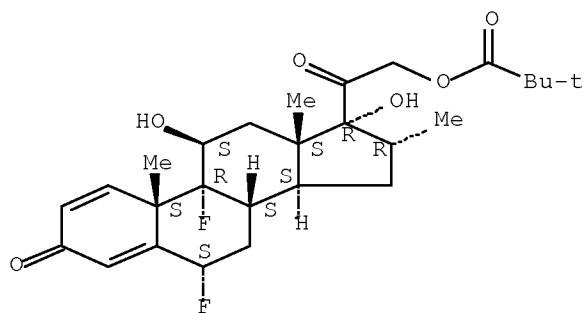


● Na

RN 2002-29-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)-6,9-difluoro-11,17-dihydroxy-16-methyl-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.



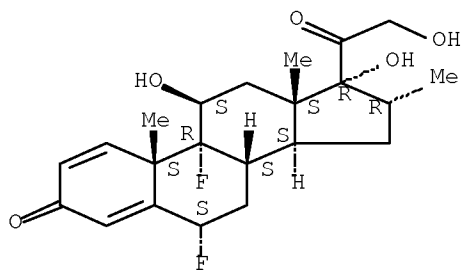
RN 2135-17-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,17,21-trihydroxy-16-methyl-,

10/524815

(6 $\alpha$ , 11 $\beta$ , 16 $\alpha$ )- (CA INDEX NAME)

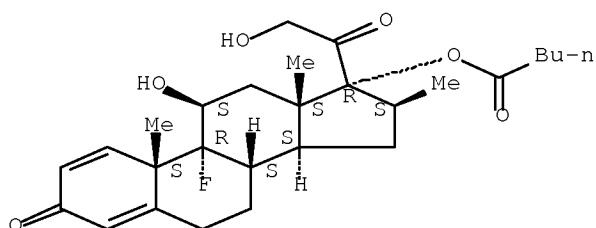
Absolute stereochemistry.



RN 2152-44-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16-methyl-17-[(1-oxopentyl)oxy]-, (11 $\beta$ , 16 $\beta$ )- (CA INDEX NAME)

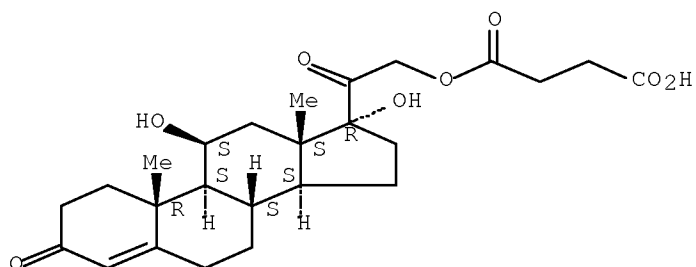
Absolute stereochemistry.



RN 2203-97-6 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

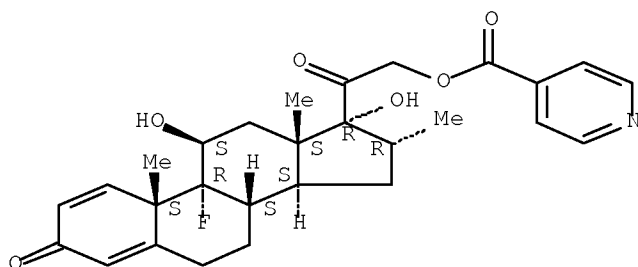


RN 2265-64-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(4-pyridinylcarbonyl)oxy]-, (11 $\beta$ , 16 $\alpha$ )- (CA INDEX NAME)

10/524815

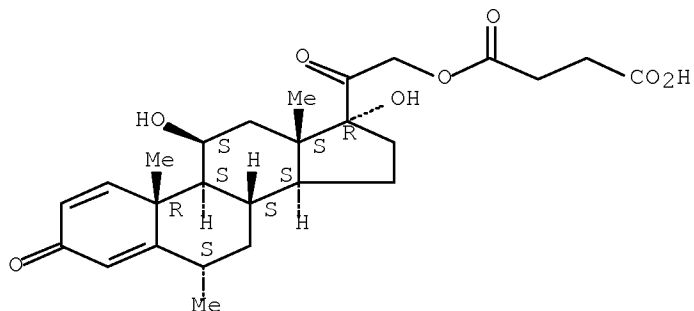
Absolute stereochemistry.



RN 2375-03-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-6-methyl-, monosodium salt, (6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

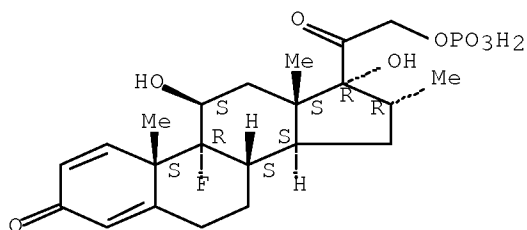


● Na

RN 2392-39-4 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-(phosphonooxy)-, sodium salt (1:2), (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.



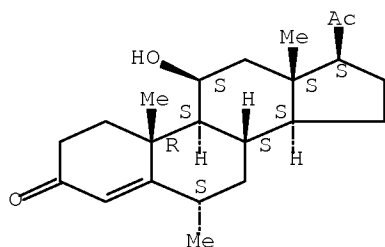
●2 Na

10/524815

RN 2668-66-8 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11-hydroxy-6-methyl-, (6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

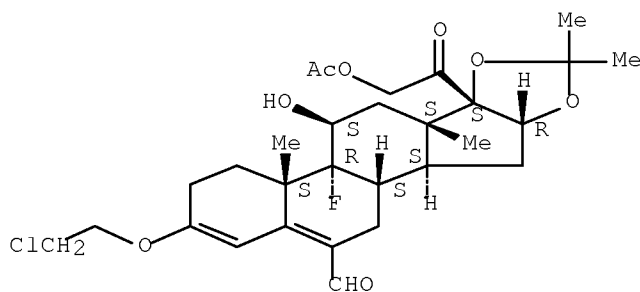
Absolute stereochemistry.



RN 2825-60-7 ZCAPLUS

CN Pregna-3,5-diene-6-carboxaldehyde, 21-(acetyloxy)-3-(2-chloroethoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-20-oxo-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

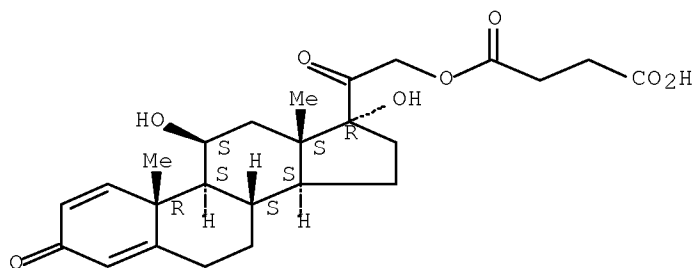
Absolute stereochemistry.



RN 2920-86-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

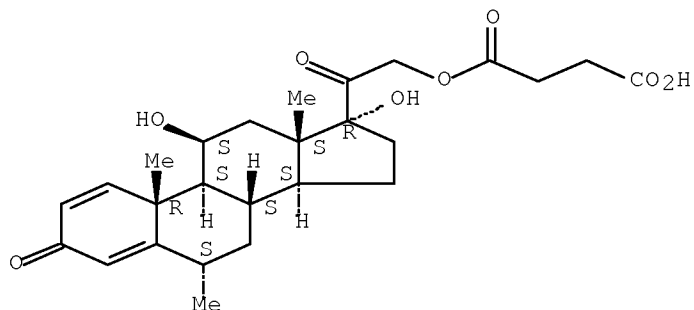


10/524815

RN 2921-57-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-6-methyl-, (6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

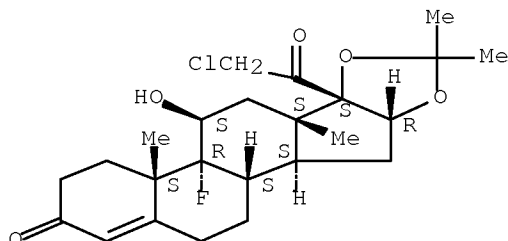
Absolute stereochemistry.



RN 3093-35-4 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-chloro-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

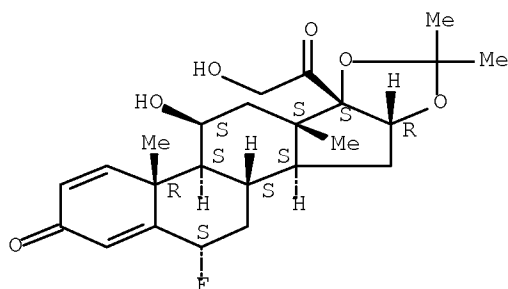
Absolute stereochemistry.



RN 3385-03-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.



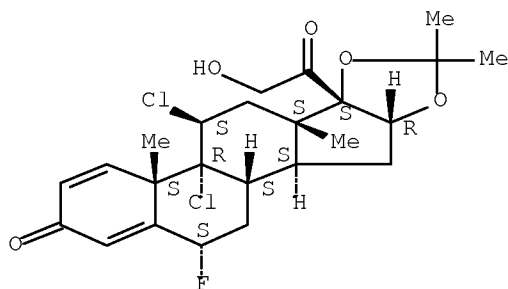


10/524815

RN 3693-39-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9,11-dichloro-6-fluoro-21-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

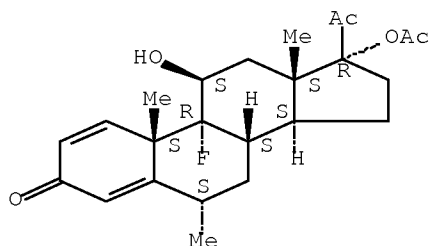
Absolute stereochemistry.



RN 3801-06-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17-(acetyloxy)-9-fluoro-11-hydroxy-6-methyl-, (6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

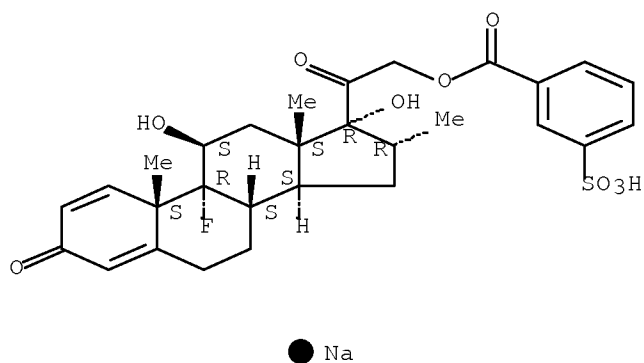


RN 3936-02-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(3-sulfobenzoyl)oxy]-, sodium salt (1:1) (CA INDEX NAME)

Absolute stereochemistry.

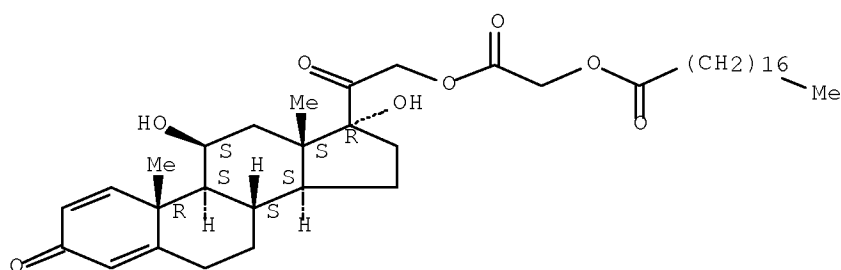
10/524815



RN 5060-55-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[[[(1-oxooctadecyl)oxy]acetyl]oxy]-, (11β)- (CA INDEX NAME)

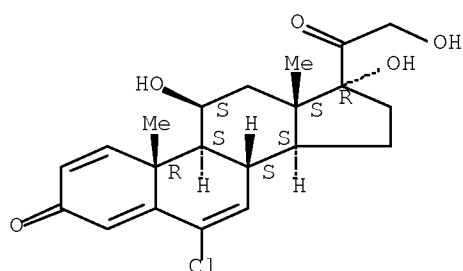
Absolute stereochemistry.



RN 5251-34-3 ZCAPLUS

CN Pregna-1,4,6-triene-3,20-dione, 6-chloro-11,17,21-trihydroxy-, (11β)- (CA INDEX NAME)

Absolute stereochemistry.

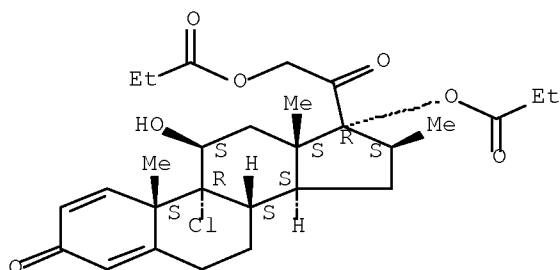


RN 5534-09-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11β,16β)- (CA INDEX NAME)

10/524815

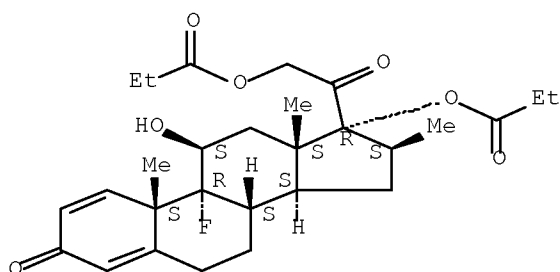
Absolute stereochemistry.



RN 5593-20-4 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

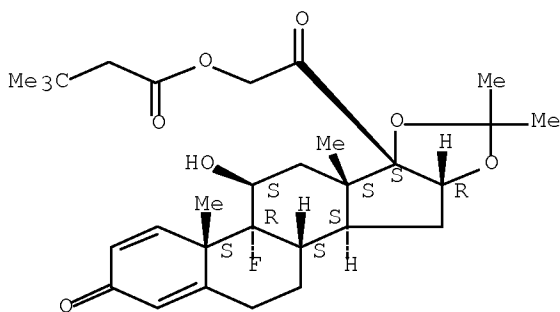
Absolute stereochemistry.



RN 5611-51-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3,3-dimethyl-1-oxobutoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.



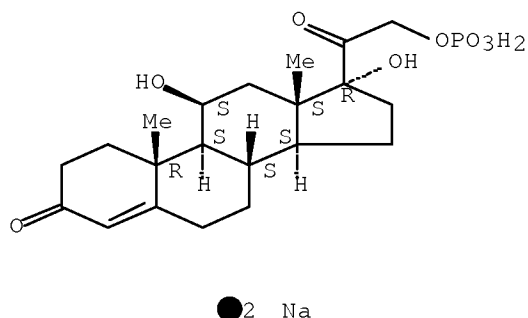
RN 6000-74-4 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-(phosphonooxy)-, sodium salt

10/524815

(1:2), (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

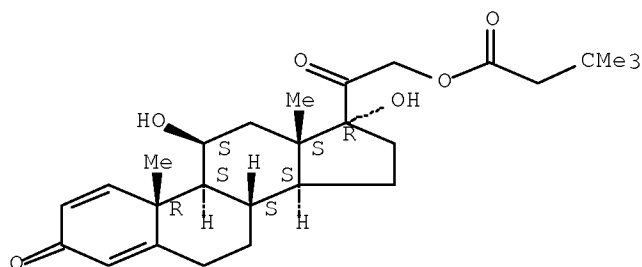


●2 Na

RN 7681-14-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3,3-dimethyl-1-oxobutoxy)-11,17-dihydroxy-, (11 $\beta$ )- (CA INDEX NAME)

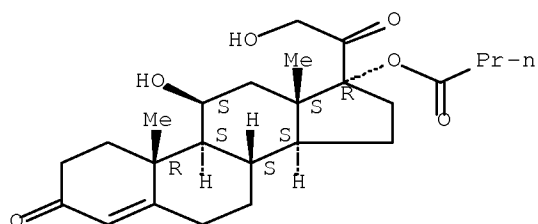
Absolute stereochemistry.



RN 13609-67-1 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,21-dihydroxy-17-(1-oxobutoxy)-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



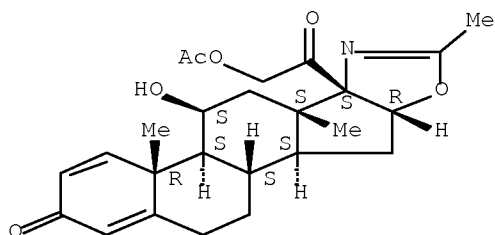
RN 14484-47-0 ZCAPLUS

CN 5'H-Pregna-1,4-dieno[17,16-d]oxazole-3,20-dione, 21-(acetyloxy)-11-hydroxy-2'-methyl-, (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

10/524815

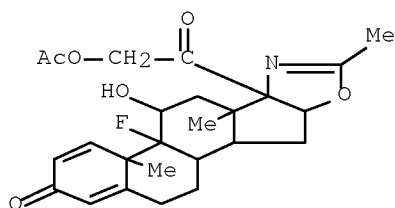
NAME)

Absolute stereochemistry.



RN 19888-56-3 ZCAPLUS

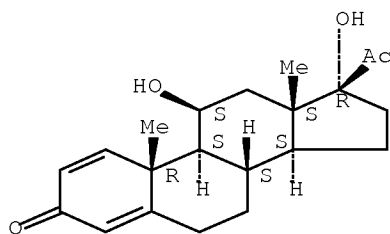
CN 5'H-Pregna-1,4-dieno[17,16-d]oxazole-3,20-dione,  
21-(acetyloxy)-9-fluoro-11-hydroxy-2'-methyl-, (11 $\beta$ ,16 $\beta$ )- (CA  
INDEX NAME)



RN 20423-99-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-, (11 $\beta$ )- (CA INDEX  
NAME)

Absolute stereochemistry.

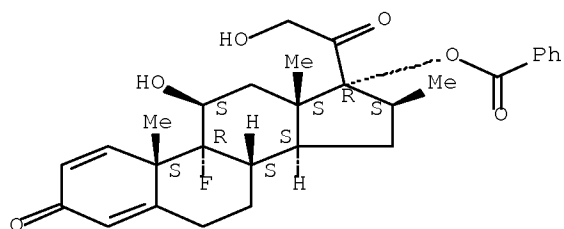


RN 22298-29-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17-(benzoyloxy)-9-fluoro-11,21-dihydroxy-16-  
methyl-, (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

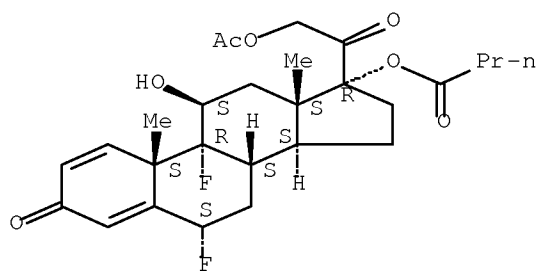
10/524815



RN 23674-86-4 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-6,9-difluoro-11-hydroxy-17-(1-oxobutoxy)-, (6 $\alpha$ ,11 $\beta$ )- (CA INDEX NAME)

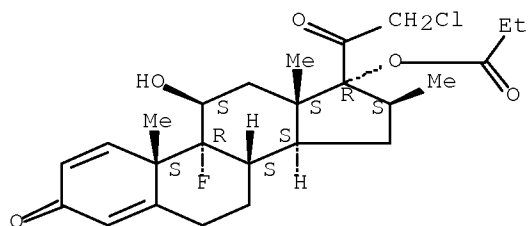
Absolute stereochemistry.



RN 25122-46-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-chloro-9-fluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-, (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

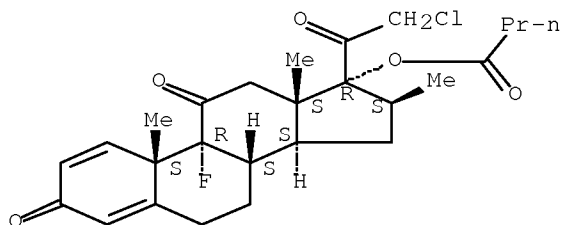


RN 25122-57-0 ZCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 21-chloro-9-fluoro-16-methyl-17-(1-oxobutoxy)-, (16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

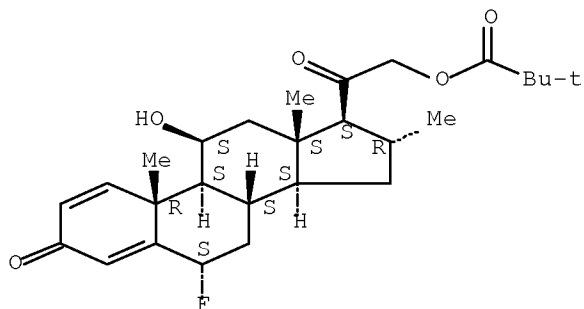
10/524815



RN 29205-06-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)-6-fluoro-11-hydroxy-16-methyl-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

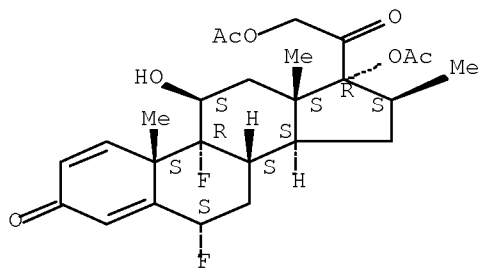
Absolute stereochemistry.



RN 33564-31-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17,21-bis(acetyloxy)-6,9-difluoro-11-hydroxy-16-methyl-, (6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

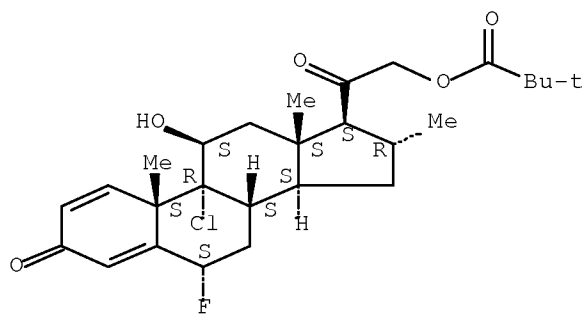


RN 34097-16-0 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-chloro-21-(2,2-dimethyl-1-oxopropoxy)-6-fluoro-11-hydroxy-16-methyl-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

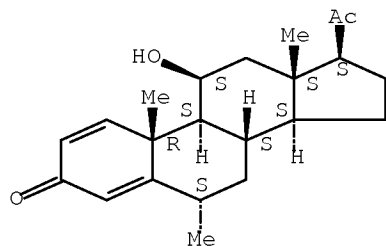
10/524815



RN 35100-44-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11-hydroxy-6-methyl-, (6 $\alpha$ ,11 $\beta$ )-  
(CA INDEX NAME)

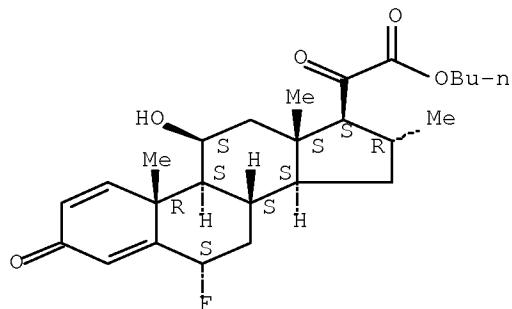
Absolute stereochemistry.



RN 41767-29-7 ZCAPLUS

CN Pregna-1,4-dien-21-oic acid, 6-fluoro-11-hydroxy-16-methyl-3,20-dioxo-,  
butyl ester, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.



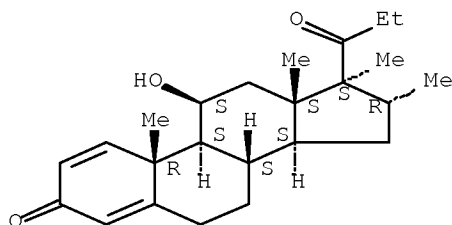
RN 49697-38-3 ZCAPLUS

CN Androsta-1,4-dien-3-one, 11-hydroxy-16,17-dimethyl-17-(1-oxopropyl)-,  
(11 $\beta$ ,16 $\alpha$ ,17 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



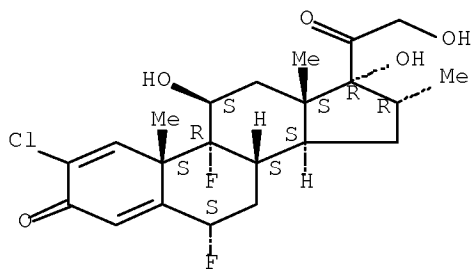
10/524815



RN 50629-82-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 2-chloro-6,9-difluoro-11,17,21-trihydroxy-16-methyl-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

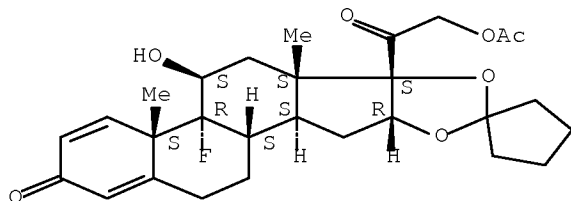
Absolute stereochemistry.



RN 51022-69-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-16,17-[cyclopentylidenebis(oxy)]-9-fluoro-11-hydroxy-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

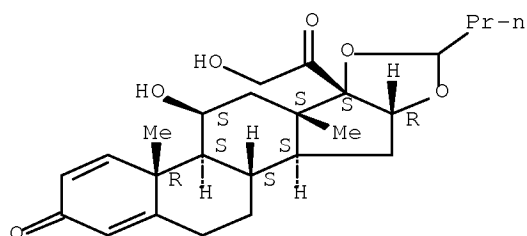


RN 51333-22-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 16,17-[butylidenebis(oxy)]-11,21-dihydroxy-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

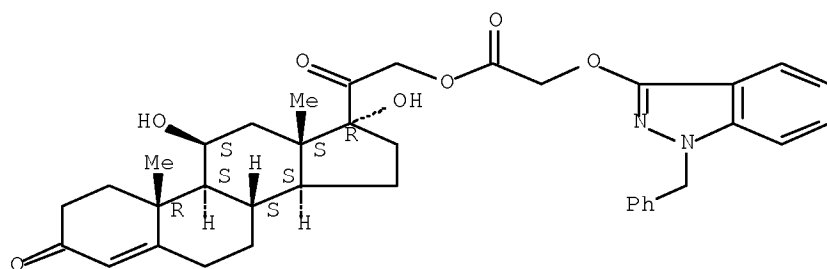
10/524815



RN 53716-43-1 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-[[2-[[1-(phenylmethyl)-1H-indazol-3-yl]oxy]acetyl]oxy]-, (11 $\beta$ )- (CA INDEX NAME)

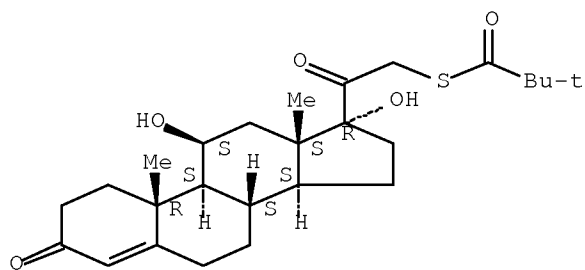
Absolute stereochemistry.



RN 55560-96-8 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-[(2,2-dimethyl-1-oxopropyl)thio]-11,17-dihydroxy-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

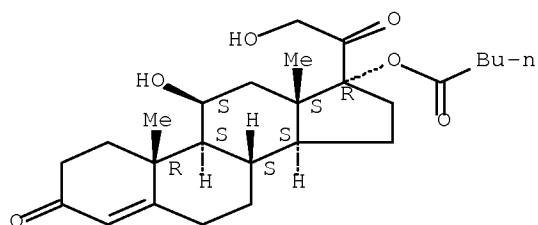


RN 57524-89-7 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,21-dihydroxy-17-[(1-oxopentyl)oxy]-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

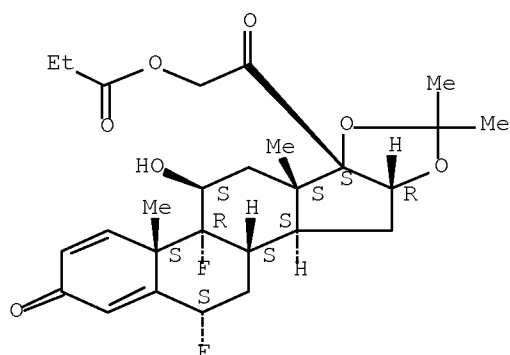
10/524815



RN 58497-00-0 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-21-(1-oxopropoxy)-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

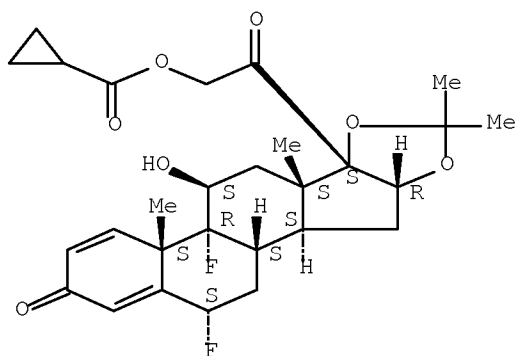
Absolute stereochemistry.



RN 58524-83-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[(cyclopropylcarbonyl)oxy]-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

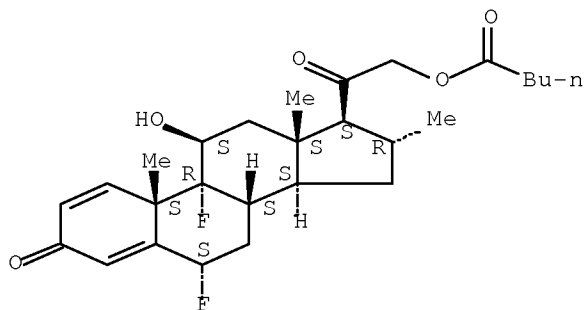


10/524815

RN 59198-70-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11-hydroxy-16-methyl-21-[(1-oxopentyl)oxy]-, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

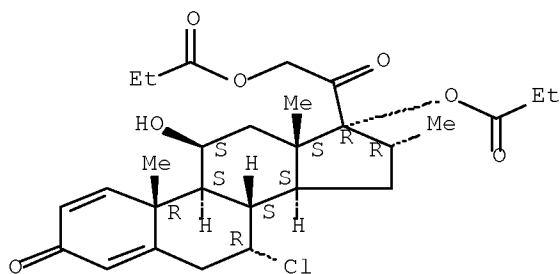
Absolute stereochemistry.



RN 66734-13-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 7-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (7 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

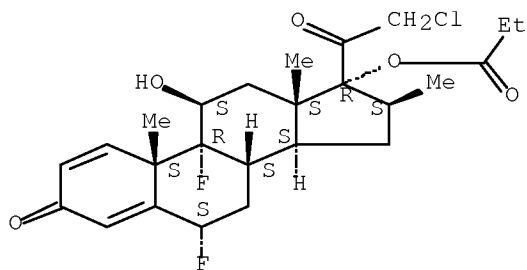
Absolute stereochemistry.



RN 66852-54-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-, (6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

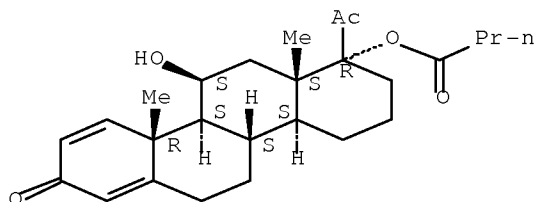


10/524815

RN 66877-67-6 ZCAPLUS

CN Butanoic acid, (1R,4aS,4bS,10aR,10bS,11S,12aS)-1-acetyl-  
1,2,3,4,4a,4b,5,6,8,10a,10b,11,12,12a-tetradecahydro-11-hydroxy-10a,12a-  
dimethyl-8-oxo-1-chrysenyl ester (CA INDEX NAME)

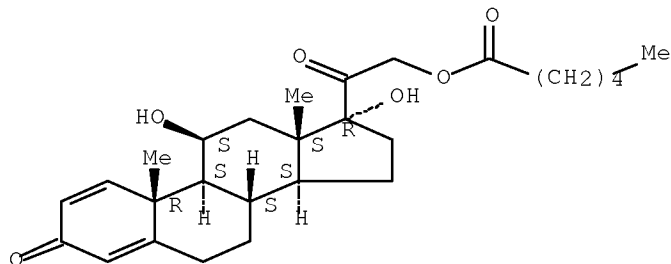
Absolute stereochemistry.



RN 69164-69-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(1-oxohexyl)oxy]-,  
(11 $\beta$ )- (CA INDEX NAME)

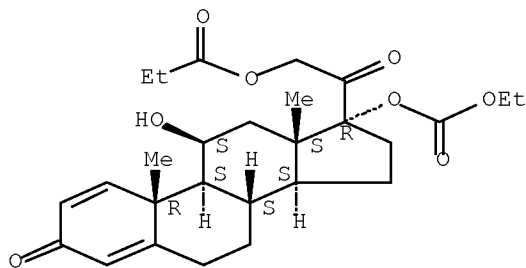
Absolute stereochemistry.



RN 73771-04-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17-[(ethoxycarbonyl)oxy]-11-hydroxy-21-(1-oxopropoxy)-, (11 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



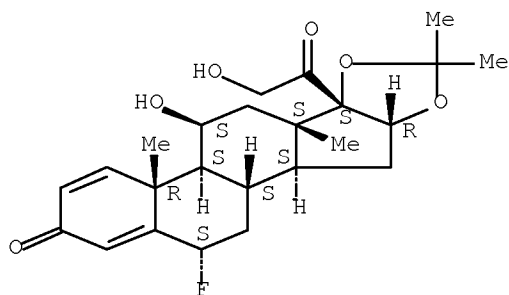
RN 77326-96-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11,21-dihydroxy-16,17-[(1-

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methylethylidene)bis(oxy)]-, hydrate (2:1), (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-  
(CA INDEX NAME)

Absolute stereochemistry.

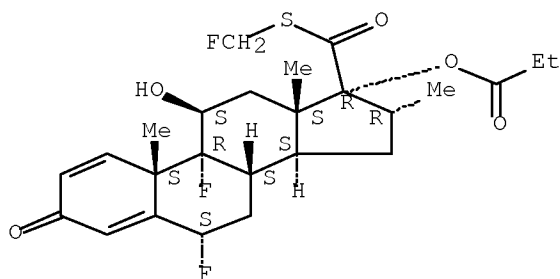


● 1/2 H<sub>2</sub>O

RN 80474-14-2 ZCAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,  
6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,  
S-(fluoromethyl) ester, (6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ ,17 $\alpha$ )- (CA  
INDEX NAME)

Absolute stereochemistry.

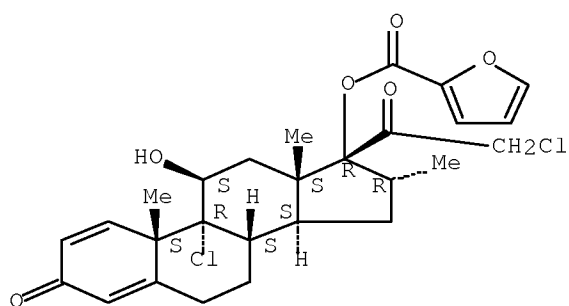


RN 83919-23-7 ZCAPLUS

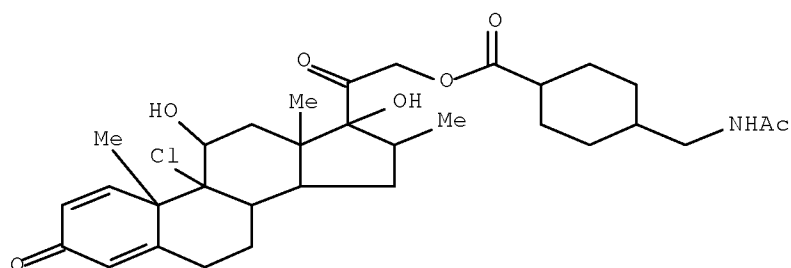
CN Pregna-1,4-diene-3,20-dione, 9,21-dichloro-17-[(2-furanylcarbonyl)oxy]-11-  
hydroxy-16-methyl-, (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry.

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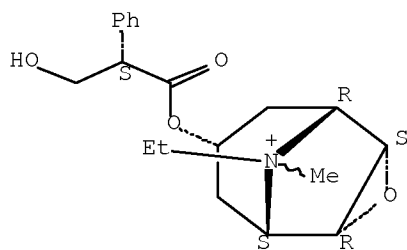


RN 86022-88-0 ZCAPLUS  
 CN Pregna-1,4-diene-3,20-dione, 21-[[[trans-4-  
 [(acetylamino)methyl]cyclohexyl]carbonyl]oxy]-9-chloro-11,17-dihydroxy-16-  
 methyl-, (11 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)



IT 30286-75-0, Oxitropium bromide 34580-13-7, Ketotifen  
 69049-74-7, Tilade 104987-11-3, FK-506  
 RL: PAC (Pharmacological activity); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (co-administration of bis(substituted phenyl)propenone VCAM-1  
 inhibitors with other biol. agents)  
 RN 30286-75-0 ZCAPLUS  
 CN 3-Oxa-9-azoniatricyclo[3.3.1.0<sup>2,4</sup>]nonane,  
 9-ethyl-7-[(2S)-3-hydroxy-1-oxo-2-phenylpropoxy]-9-methyl-, bromide (1:1),  
 (1 $\alpha$ ,2 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,7 $\beta$ )- (CA INDEX NAME)

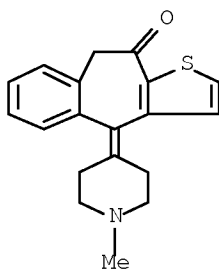
Absolute stereochemistry.



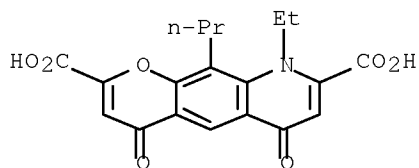
● Br<sup>-</sup>

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RN 34580-13-7 ZCAPLUS  
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one,  
4,9-dihydro-4-(1-methyl-4-piperidinylidene)- (CA INDEX NAME)



RN 69049-74-7 ZCAPLUS  
CN 4H-Pyrano[3,2-g]quinoline-2,8-dicarboxylic acid,  
9-ethyl-6,9-dihydro-4,6-dioxo-10-propyl-, sodium salt (1:2) (CA INDEX NAME)

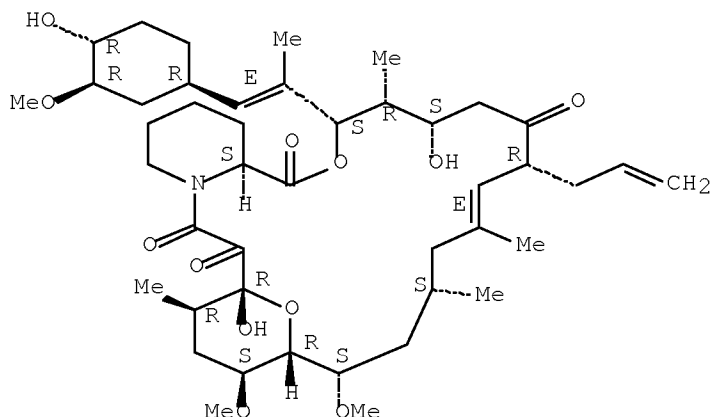


● 2 Na

RN 104987-11-3 ZCAPLUS  
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-  
tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-  
dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-  
methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propen-1-yl)-,  
(3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.





OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
(4 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 7 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:420941 ZCAPLUS Full-text

DOCUMENT NUMBER: 133:53696

TITLE: Tricyclic nitrogen heterocycles as phosphodiesterase  
IV inhibitors

INVENTOR(S): Hoffmann, Matthias; Jung, Birgit; Kuefner-Muehl,  
Ulrike; Meade, Christopher John Montague

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

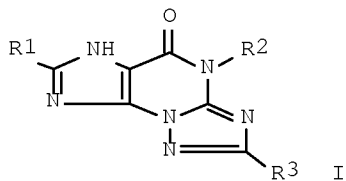
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035428	A2	20000622	WO 1999-EP9086	19991124 <--
WO 2000035428	A3	20000928		
W: CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19858331	A1	20000621	DE 1998-19858331	19981217 <--
CA 2345752	A1	20000622	CA 1999-2345752	19991124 <--
EP 1140098	A2	20011010	EP 1999-959324	19991124 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6417190	B1	20020709	US 1999-458789	19991210 <--
MX 2001005936	A	20011203	MX 2001-5936	20010612 <--
PRIORITY APPLN. INFO.:				
			DE 1998-19858331	A 19981217 <--
			US 1999-127777P	P 19990405 <--
			WO 1999-EP9086	W 19991124 <--

OTHER SOURCE(S): MARPAT 133:53696  
GI



- AB    **Tricyclic N heterocycles I** [R1 = C1-5 alkyl, C5-6 cycloalkyl, Ph, PhCH<sub>2</sub>, 5- or 6-membered heterocyclic ring; R2 = C1-5 alkyl, C2-4 alkenyl; R3 = (substituted) C1-5 alkyl, (substituted) C5-6 cycloalkyl] and their salts are phosphodiesterase IV inhibitors and are potentially useful as vasodilators, inflammation inhibitors, and antiallergic agents. Thus, I (R1 = cyclopentyl, R2 = n-Pr, R3 = i-Pr) inhibited human monocyte phosphodiesterase IV with an IC<sub>50</sub> of 0.018  $\mu$ m. A tablet formulation contained I 80, corn starch 190, lactose 55, microcryst. cellulose 35, PVP 15, Na carboxymethylstarch 23, and Mg stearate 2 mg.
- IC    ICM   A61K031-00
- CC    1-7 (Pharmacology)
- Section cross-reference(s): 7, 63
- IT    Intestine, disease  
       (Crohn's; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Respiratory distress syndrome  
       (adult; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Eye, disease  
       (allergic conjunctivitis; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Tumor necrosis factors  
       RL: BSU (Biological study, unclassified); BIOL (Biological study)  
       (antagonists; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Bronchi  
       (chronic bronchitis; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Kidney, disease  
       (chronic glomerulonephritis; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Lung, disease  
       (chronic obstructive; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Granuloma  
       (eosinophilic; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Lung, disease  
       Respiratory tract  
       (inflammation; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Structure-activity relationship  
       (phosphodiesterase IV-inhibiting; of **tricyclic nitrogen heterocycles**)
- IT    Shock (circulatory collapse)  
       (septic; **tricyclic nitrogen heterocycles** as phosphodiesterase IV inhibitors)
- IT    Allergy inhibitors

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Anti-inflammatory agents

Anti-ischemic agents

Antiarteriosclerotics

Antiarthritics

Antiasthmatics

Antirheumatic agents

Cystic fibrosis

Eye, disease

Hay fever

Multiple sclerosis

Psoriasis

Urticaria

(tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)

IT Intestine, disease

(ulcerative colitis; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)

IT 9036-21-9, Phosphodiesterase IV

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)

IT 60-92-4, CAMP

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (intracellular; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)

IT 252665-20-6 252665-32-0 252665-46-6 252665-52-4 259744-63-3

259744-64-4 259744-65-5 259744-67-7 259744-68-8

259744-69-9 259744-82-6 259744-83-7 259744-90-6 259744-91-7

259744-95-1 259745-04-5 259745-05-6 259745-08-9 259745-18-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)

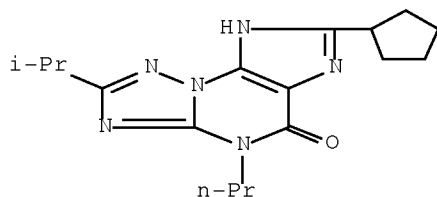
IT 259744-67-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)

RN 259744-67-7 ZCAPLUS

CN 5H-[1,2,4]Triazolo[5,1-b]purin-5-one, 7-cyclopentyl-4,8-dihydro-2-(1-methylethyl)-4-propyl- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

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REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his full

(FILE 'HOME' ENTERED AT 09:55:10 ON 14 OCT 2009)

FILE 'REGISTRY' ENTERED AT 09:55:15 ON 14 OCT 2009

L1 0 SEA SPE=ON ABB=ON PLU=ON AMITRYPTILINE/CN  
L2 1 SEA SPE=ON ABB=ON PLU=ON IMIPRAMINE/CN  
D SCA  
L3 1 SEA SPE=ON ABB=ON PLU=ON AMITRIPTYLINE/CN  
D SCA  
SEL RN  
D RN L2  
D RN L3  
L4 STR 50-49-7  
L5 STR 50-48-6  
L6 4 SEA FAM SAM L4  
L7 135 SEA FAM FUL L4  
L8 3 SEA FAM SAM L5  
L9 83 SEA FAM FUL L5  
SAVE TEMP L7 JEA815IMIP/A  
SAVE TEMP L9 JEA815AMIT/A

FILE 'ZCAPLUS' ENTERED AT 10:00:52 ON 14 OCT 2009

L10 9293 SEA SPE=ON ABB=ON PLU=ON L7  
L11 6299 SEA SPE=ON ABB=ON PLU=ON L9  
E ANTIDEPRESSANT+ALL/CT  
E E2+ALL/CT

FILE 'REGISTRY' ENTERED AT 10:07:23 ON 14 OCT 2009

L12 6 SEA SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR CLOMIPRAMINE OR  
DOSULEPIN OR DOTHIEPIN OR DOXEPIN OR LOFEPRAMINE OR TRIMIPRAMIN  
E)/CN  
D SCA  
L13 3 SEA SPE=ON ABB=ON PLU=ON (DESIPRAMINE OR NORTRIPTYLINE OR  
PROTRIPTYLINE)/CN  
L14 6 SEA SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR DIBENZEPIN OR  
DIMETACRINE OR IPRINDOLE OR MELITRACEN OR METAPRAMINE)/CN  
L15 4 SEA SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR NOXIPTILINE OR  
PROPIZEPINE OR QUINUPRAMINE)/CN  
L16 6 SEA SPE=ON ABB=ON PLU=ON (AMINEPTINE OR OPIPRAMOL OR  
TIANEPTINE OR CIANOPRAMINE OR CYANODOTHIEPIN OR FLUOTRACEN)/CN  
L17 25 SEA SPE=ON ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR L16)  
L18 25 SEA SPE=ON ABB=ON PLU=ON L17 NOT (L7 OR L9)  
D SCA  
L19 6 SEA SPE=ON ABB=ON PLU=ON (AMOXAPINE OR MAPROTILINE OR  
MIANSERIN OR MIRTAPAZINE OR SETIPTILINE OR OXAPROTILINE)/CN  
L20 0 SEA SPE=ON ABB=ON PLU=ON L18 AND L19  
D COST

FILE 'ZCAPLUS' ENTERED AT 10:16:36 ON 14 OCT 2009

E TRICYCLIC ANTI/CT  
E E4+ALL/CT  
E E2+ALL/CT  
L21 5776 SEA SPE=ON ABB=ON PLU=ON ANTIDEPRESS?/BI (L) TRICYCLIC?/BI  
E TETRACYCLIC ANTI/CT  
L22 270 SEA SPE=ON ABB=ON PLU=ON ANTIDEPRESS?/BI (L) TETRACYCLIC?/BI  
L23 36339 SEA SPE=ON ABB=ON PLU=ON ANTIDEPRESSANT?/BI OR ANTI

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DEPRESSANT?/BI
E CYSTIC FIBROSIS+ALL/CT
L24      15309 SEA SPE=ON  ABB=ON  PLU=ON  ?CYSTIC FIBROS?/BI
L*** DEL  608 S FIBROCYSTIC/BI OR FIBROCYSTIC/BI
L25      609 SEA SPE=ON  ABB=ON  PLU=ON  FIBROCYSTIC?/BI OR FIBRO CYSTIC?/BI

L26      155 SEA SPE=ON  ABB=ON  PLU=ON  MUCOVISCIDOSIS/BI
L27      5892 SEA SPE=ON  ABB=ON  PLU=ON  CFTR/BI
L28      15430 SEA SPE=ON  ABB=ON  PLU=ON  FIBROSIS/BI (L) CYSTIC/BI
L29      16341 SEA SPE=ON  ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28)
L30      226 SEA SPE=ON  ABB=ON  PLU=ON  (L21 OR L22 OR L23) AND L29
L31      6 SEA SPE=ON  ABB=ON  PLU=ON  (L21 OR L22) AND L29
L32      9 SEA SPE=ON  ABB=ON  PLU=ON  L23 AND (TRICYCLIC?/BI OR
TETRACYCLIC?/BI) AND L29
L33      3 SEA SPE=ON  ABB=ON  PLU=ON  L32 NOT L31
D SCA

FILE 'REGISTRY' ENTERED AT 10:28:51 ON 14 OCT 2009
L34      31 SEA SPE=ON  ABB=ON  PLU=ON  L17 OR L19
L35      31 SEA SPE=ON  ABB=ON  PLU=ON  L34 NOT (L7 OR L9)

FILE 'ZCAPLUS' ENTERED AT 10:29:09 ON 14 OCT 2009
L36      11 SEA SPE=ON  ABB=ON  PLU=ON  L34 AND L29
L37      12 SEA SPE=ON  ABB=ON  PLU=ON  (L7 OR L9) AND L29
L38      9 SEA SPE=ON  ABB=ON  PLU=ON  L36 AND L37

FILE 'REGISTRY' ENTERED AT 10:40:10 ON 14 OCT 2009
L39      22 SEA SPE=ON  ABB=ON  PLU=ON  L17 AND 3/NR
L40      3 SEA SPE=ON  ABB=ON  PLU=ON  L17 NOT L39
D SCA
L41      6 SEA SPE=ON  ABB=ON  PLU=ON  L19 AND 4/NR
D SCA

FILE 'ZCAPLUS' ENTERED AT 10:45:18 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:46:24 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 10:46:38 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:48:01 ON 14 OCT 2009
L*** DEL  TRA L29 1- RN : 50127 TERMS

FILE 'REGISTRY, REGISTRY' ENTERED AT 10:48:01 ON 14 OCT 2009
L*** DEL  50126 SEA L***

FILE 'ZCAPLUS' ENTERED AT 10:50:34 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:50:56 ON 14 OCT 2009
L45      218 SEA SPE=ON  ABB=ON  PLU=ON  L7 OR L9

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:52:26 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:52:31 ON 14 OCT 2009
SET SMARTSELECT ON
L46      SEL PLU=ON  L45 1- CHEM : 409 TERMS
SET SMARTSELECT OFF

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:53:03 ON 14 OCT 2009
L47      78135 SEA SPE=ON  ABB=ON  PLU=ON  L46
L48      96337 SEA SPE=ON  ABB=ON  PLU=ON  L29
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L49          39 SEA SPE=ON  ABB=ON  PLU=ON  L47 AND L48
L50          36 DUP REM L49 (3 DUPLICATES REMOVED)
              ANSWERS '1-5' FROM FILE MEDLINE
              ANSWERS '6-34' FROM FILE EMBASE
              ANSWERS '35-36' FROM FILE BIOSIS

FILE 'EMBASE' ENTERED AT 10:55:22 ON 14 OCT 2009
L51          31 SEA SPE=ON  ABB=ON  PLU=ON  L47 AND L48
              D TRIAL 1-6

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:56:20 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:57:04 ON 14 OCT 2009
              SET SMARTSELECT ON
L52          SEL PLU=ON  L34 1- CHEM :      233 TERMS
              SET SMARTSELECT OFF

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:57:06 ON 14 OCT 2009
L53          91067 SEA SPE=ON  ABB=ON  PLU=ON  L52
L*** DEL      2 S L53 AND L@9
L54          25 SEA SPE=ON  ABB=ON  PLU=ON  L53 AND L29
              D TRIAL 1-5
L55          54 SEA SPE=ON  ABB=ON  PLU=ON  L49 OR L54
L56          24 SEA SPE=ON  ABB=ON  PLU=ON  (TRICYCLIC OR TETRACYCLIC)/BI AND
              L29
L57          75 SEA SPE=ON  ABB=ON  PLU=ON  L49 OR L54 OR L56
              D TRIAL L56 1-5
              D TRIAL L56 6-10
L58          31 SEA SPE=ON  ABB=ON  PLU=ON  L57 AND PY<2004

FILE 'ZCAPLUS' ENTERED AT 11:05:19 ON 14 OCT 2009
L59          27 SEA SPE=ON  ABB=ON  PLU=ON  (TRICYCLIC?/BI OR  TETRACYCLIC?/BI)
              AND L29
L60          7 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND PY<2004
L61          15 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND PRY<2004
L62          13 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND AY<2004
L63          17 SEA SPE=ON  ABB=ON  PLU=ON  (L60 OR L61 OR L62)
              SEL RN
              DELETE SELECT
              SEL RN

FILE 'REGISTRY' ENTERED AT 11:09:34 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:09:41 ON 14 OCT 2009
L64          TRA PLU=ON  L63 1- RN :      3492 TERMS

FILE 'REGISTRY' ENTERED AT 11:09:43 ON 14 OCT 2009
L65          3492 SEA SPE=ON  ABB=ON  PLU=ON  L64
L66          1346 SEA SPE=ON  ABB=ON  PLU=ON  L65 AND NRRS>2

FILE 'ZCAPLUS' ENTERED AT 11:10:02 ON 14 OCT 2009
L67          4889 SEA SPE=ON  ABB=ON  PLU=ON  L66 AND ?DEPRESS?/BI

FILE 'REGISTRY' ENTERED AT 11:11:02 ON 14 OCT 2009
L68          1330 SEA SPE=ON  ABB=ON  PLU=ON  L66 AND NRRS<5

FILE 'ZCAPLUS' ENTERED AT 11:11:26 ON 14 OCT 2009
L69          40308 SEA SPE=ON  ABB=ON  PLU=ON  L66 (L) (THU OR DMA OR PAC OR PKT
              OR BAC)/RL
L70          788 SEA SPE=ON  ABB=ON  PLU=ON  L69 AND (?DEPRESSION? OR ?ANTIDEPRE
```

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SS? OR ANTI DEPRESS?)/BI  
L71 ANALYZE PLU=ON L70 1- RN HIT : 344 TERMS  
DELETE SELECT Y  
SEL 1-344

FILE 'REGISTRY' ENTERED AT 11:15:14 ON 14 OCT 2009

L72 344 SEA SPE=ON ABB=ON PLU=ON (50-02-2/RN OR 50-23-7/RN OR  
53-03-2/RN OR 50-24-8/RN OR 104987-11-3/RN OR 79794-75-5/RN OR  
60-87-7/RN OR 83-43-2/RN OR 51333-22-3/RN OR 378-44-9/RN OR  
76-25-5/RN OR 124-94-7/RN OR 5534-09-8/RN OR 3385-03-3/RN OR  
356-12-7/RN OR 80474-14-2/RN OR 25122-46-7/RN OR 50-03-3/RN OR  
67-73-2/RN OR 382-67-2/RN OR 1247-42-3/RN OR 3093-35-4/RN OR  
426-13-1/RN OR 638-94-8/RN OR 2152-44-5/RN OR 1524-88-5/RN OR  
34580-13-7/RN OR 33564-31-7/RN OR 52-39-1/RN OR 67-78-7/RN OR  
50-04-4/RN OR 51022-69-6/RN OR 2668-66-8/RN OR 49697-38-3/RN  
OR 66575-29-9/RN OR 83919-23-7/RN OR 969-33-5/RN OR 13609-67-1/  
RN OR 152-97-6/RN OR 2135-17-3/RN OR 53-34-9/RN OR 53-36-1/RN  
OR 23674-86-4/RN OR 5593-20-4/RN OR 57524-89-7/RN OR 125-02-0/R  
N OR 2002-29-1/RN OR 2375-03-3/RN OR 3693-39-8/RN OR 66734-13-2  
/RN OR 41767-29-7/RN OR 508-99-6/RN OR 52-21-1/RN OR 125-04-2/R  
N OR 14484-47-0/RN OR 56-47-3/RN OR 59198-70-8/RN OR 73771-04-7  
/RN OR 987-24-6/RN OR 25122-57-0/RN OR 30286-75-0/RN OR  
312-93-6/RN OR 3801-06-7/RN OR 1110-40-3/RN OR 1255-35-2/RN OR  
1597-82-6/RN OR 22298-29-9/RN OR 2825-60-7/RN OR 514-36-3/RN  
OR 5611-51-8/RN OR 599-33-7/RN OR 66852-54-8/RN OR 69049-74-7/R  
N OR 82-88-2/RN OR 1177-87-3/RN OR 19888-56-3/RN OR 34097-16-0/  
RN OR 50629-82-8/RN OR 5251-34-3/RN OR 4330-99-8/RN OR  
151-73-5/RN OR 2392-39-4/RN OR 55560-96-8/RN OR 7681-14-3/RN  
OR 86-74-8/RN OR 1229-35-2/RN OR 2920-86-7/RN OR 35100-44-8/RN  
OR 58497-00-0/RN OR 58524-83-7/RN OR 6000-74-4/RN OR 1107-99-9/  
RN OR 125-03-1/RN OR 125-10-0/RN OR 132-65-0/RN OR 1715-33-9/RN  
OR 20423-99-8/RN OR 2265-64-7/RN OR 29205-06-9/RN OR 2921-57-5  
/RN OR 303-40-2/RN OR 5060-55-9/RN OR 630-67-1/RN OR 778576-34-  
4/RN OR 778576-35-5/RN OR 778576-36-6/RN OR 778576-37-7/RN OR  
778576-38-8/RN OR 778576-39-9/RN OR 778576-40-2/RN OR 778576-41  
-3/RN OR 778576-42-4/RN O

FILE 'ZCAPLUS' ENTERED AT 11:15:54 ON 14 OCT 2009

L73 8 SEA SPE=ON ABB=ON PLU=ON L72 AND L63  
D OCC 1-  
L74 7 SEA SPE=ON ABB=ON PLU=ON (L72 (L) (THU OR DMA OR BAC OR PKT  
OR PAC)/RL) AND L63  
D OCC 1-  
D SCA  
L75 227 SEA SPE=ON ABB=ON PLU=ON GULBINS E?/AU,AUTH  
L76 6 SEA SPE=ON ABB=ON PLU=ON L75 AND (L7 OR L9 OR L17 OR L19)  
L77 18 SEA SPE=ON ABB=ON PLU=ON L75 AND L29

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:20:43 ON 14 OCT 2009

L78 24 SEA SPE=ON ABB=ON PLU=ON L75 AND (L47 OR L53)  
L79 48 SEA SPE=ON ABB=ON PLU=ON L75 AND L29  
L80 64 SEA SPE=ON ABB=ON PLU=ON L78 OR L79  
L81 32 DUP REM L80 (32 DUPLICATES REMOVED)  
ANSWERS '1-21' FROM FILE MEDLINE  
ANSWERS '22-24' FROM FILE EMBASE  
ANSWERS '25-32' FROM FILE BIOSIS

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:22:08 ON 14 OCT 2009

L82 8 SEA SPE=ON ABB=ON PLU=ON L57 AND L75



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FILE 'ZCAPLUS' ENTERED AT 11:22:35 ON 14 OCT 2009  
L83 14 SEA SPE=ON ABB=ON PLU=ON L75 AND L32 OR L36 OR L37  
L84 2 SEA SPE=ON ABB=ON PLU=ON L75 AND (L32 OR L36 OR L37)  
L85 0 SEA SPE=ON ABB=ON PLU=ON L75 AND L74  
L86 0 SEA SPE=ON ABB=ON PLU=ON L59 AND L75

FILE 'REGISTRY' ENTERED AT 11:24:11 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:24:13 ON 14 OCT 2009  
D STAT QUE L76  
D STAT QUE L77  
D STAT QUE L84  
L87 22 SEA SPE=ON ABB=ON PLU=ON L76 OR L77 OR L84

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:24:54 ON 14 OCT 2009  
D STAT QUE L78  
D STAT QUE L79  
D STAT QUE L82  
L88 64 SEA SPE=ON ABB=ON PLU=ON L78 OR L79 OR L82

FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:25:25 ON 14 OCT 2009  
L89 37 DUP REM L87 L88 (49 DUPLICATES REMOVED)  
ANSWERS '1-22' FROM FILE ZCAPLUS  
ANSWERS '23-29' FROM FILE MEDLINE  
ANSWERS '30-32' FROM FILE EMBASE  
ANSWERS '33-37' FROM FILE BIOSIS  
D IBIB ABS HITIND HITSTR L89 1-22  
D IALL L89 23-37

FILE 'REGISTRY' ENTERED AT 11:26:43 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:26:46 ON 14 OCT 2009  
D STAT QUE L32  
D STAT QUE L36  
D STAT QUE L37  
L90 22 SEA SPE=ON ABB=ON PLU=ON L32 OR L36 OR L37

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:27:21 ON 14 OCT 2009  
D STAT QUE L58

FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:27:33 ON 14 OCT 2009  
L91 49 DUP REM L90 L58 (4 DUPLICATES REMOVED)  
ANSWERS '1-22' FROM FILE ZCAPLUS  
ANSWERS '23-27' FROM FILE MEDLINE  
ANSWERS '28-48' FROM FILE EMBASE  
ANSWER '49' FROM FILE BIOSIS  
D IBIB ABS HITIND HITSTR L91 1-22  
D IALL L91 23-49

FILE 'REGISTRY' ENTERED AT 11:28:47 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:28:55 ON 14 OCT 2009  
D STAT QUE L74  
D IBIB ABS HITIND HITSTR L74 1-7

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file

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provided by InfoChem.

STRUCTURE FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6  
DICTIONARY FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

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predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

#### FILE ZCAPLUS

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FILE COVERS 1907 - 14 Oct 2009 VOL 151 ISS 16  
FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

ZCAplus now includes complete International Patent Classification (IPC)  
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

#### FILE MEDLINE

FILE LAST UPDATED: 13 Oct 2009 (20091013/UP). FILE COVERS 1949 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2009 Medical Subject  
Headings (MeSH) vocabulary and tree numbers from the U.S. National Library  
of Medicine (NLM). Additional information is available at

[http://www.nlm.nih.gov/pubs/techbull/nd08/nd08\\_medline\\_data\\_changes\\_2009](http://www.nlm.nih.gov/pubs/techbull/nd08/nd08_medline_data_changes_2009).

On February 21, 2009, MEDLINE was reloaded. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

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See HELP RANGE before carrying out any RANGE search.

FILE EMBASE

FILE COVERS 1974 TO 14 Oct 2009 (20091014/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE BIOSIS

FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 7 October 2009 (20091007/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

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